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<p>(21) International Application Number: PCT/US00/09312</p> <p>(22) International Filing Date: 7 April 2000 (07.04.00)</p> <p>(30) Priority Data:</p> <table border="0"> <tr> <td>09/289,198</td> <td>9 April 1999 (09.04.99)</td> <td>US</td> </tr> <tr> <td>09/429,755</td> <td>28 October 1999 (28.10.99)</td> <td>US</td> </tr> <tr> <td>09/534,825</td> <td>23 March 2000 (23.03.00)</td> <td>US</td> </tr> </table> <p>(71) Applicant: CORIXA CORPORATION [US/US]; Suite 200, 1124 Columbia Street, Seattle, WA 98104 (US).</p> <p>(72) Inventors: FRUDAKIS, Tony, N.; 7937 Broadmoor Pines Boulevard, Sarasota, FL 34243 (US). SMITH, John, M.; 208 - 116th Place S.E., Everett, WA 98208 (US). REED, Steven, G.; 2843 - 122nd Place N.E., Bellevue, WA 98005 (US). MISHER, Lynda, E.; 6251 53rd Avenue N.E., Seattle, WA 98115 (US). RETTER, Marc, W.; 33402 N.E. 43rd Place, Carnation, WA 98014 (US). DILLON, Davin, C.; 21607 N.E. 24th Street, Redmond, WA 98053 (US).</p> <p>(74) Agents: POTTER, Jane, E., R.; Seed Intellectual Property Law Group PLLC, Suite 6300, 701 Fifth Avenue, Seattle, WA 98104-7092 (US) et al.</p>		09/289,198	9 April 1999 (09.04.99)	US	09/429,755	28 October 1999 (28.10.99)	US	09/534,825	23 March 2000 (23.03.00)	US	<p>(81) Designated States: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, ARIPO patent (GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).</p> <p>Published <i>Without international search report and to be republished upon receipt of that report.</i></p>
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<p>(54) Title: COMPOSITIONS AND METHODS FOR THE TREATMENT AND DIAGNOSIS OF BREAST CANCER</p> <div style="text-align: center;">  </div> <p>(57) Abstract</p> <p>Compositions and methods for the detection and therapy of breast cancer are disclosed. The compounds provided include nucleotide sequences that are preferentially expressed in breast tumor tissue, as well as polypeptides encoded by such nucleotide sequences. Vaccines and pharmaceutical compositions comprising such compounds are also provided and may be used, for example, for the prevention and treatment of breast cancer. The polypeptides may also be used for the production of antibodies, which are useful for diagnosing and monitoring the progression of breast cancer in a patient.</p>											

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COMPOSITIONS AND METHODS FOR THE TREATMENT AND DIAGNOSIS OF BREAST CANCER

TECHNICAL FIELD

The present invention relates generally to the detection and therapy of breast cancer. The invention is more specifically related to nucleotide sequences that are preferentially expressed in breast tumor tissue and to polypeptides encoded by such nucleotide sequences. The nucleotide sequences and polypeptides may be used in vaccines and pharmaceutical compositions for the prevention and treatment of breast cancer. The polypeptides may also be used for the production of compounds, such as antibodies, useful for diagnosing and monitoring the progression of breast cancer in a patient.

BACKGROUND OF THE INVENTION

Breast cancer is a significant health problem for women in the United States and throughout the world. Although advances have been made in detection and treatment of the disease, breast cancer remains the second leading cause of cancer-related deaths in women, affecting more than 180,000 women in the United States each year. For women in North America, the life-time odds of getting breast cancer are now one in eight.

No vaccine or other universally successful method for the prevention or treatment of breast cancer is currently available. Management of the disease currently relies on a combination of early diagnosis (through routine breast screening procedures) and aggressive treatment, which may include one or more of a variety of treatments such as surgery, radiotherapy, chemotherapy and hormone therapy. The course of treatment for a particular breast cancer is often selected based on a variety of prognostic parameters, including an analysis of specific tumor markers. See, e.g., Porter-Jordan and Lippman, *Breast Cancer* 8:73-100 (1994). However, the use of established markers often leads to a result that is difficult to interpret, and the high mortality observed in

breast cancer patients indicates that improvements are needed in the treatment, diagnosis and prevention of the disease.

Accordingly, there is a need in the art for improved methods for therapy and diagnosis of breast cancer. The present invention fulfills these needs and further provides other related advantages.

SUMMARY OF THE INVENTION

Briefly stated, the subject invention provides compositions and methods for the diagnosis and therapy of breast cancer. In one aspect, isolated polynucleotides are provided, comprising (a) a nucleotide sequence preferentially expressed in breast cancer tissue, relative to normal tissue; (b) a variant of such a sequence, as defined below; or (c) a nucleotide sequence encoding an epitope of a polypeptide encoded by at least one of the above sequences. In one embodiment, the isolated polynucleotide comprises a human endogenous retroviral sequence recited in SEQ ID NO:1. In other embodiments, the isolated polynucleotide comprises a sequence recited in any one of SEQ ID NO: 3-26, 28-77, 142, 143, 146-152, 154-166, 168-176, 178-192, 194-198, 200-204, 206, 207, 209-214, 216, 218, 219, 221-240, 243-245, 247, 250, 251, 253, 255, 257-266, 268, 269, 271-273, 275, 276, 278, 280, 281, 284, 288, 291-298, 301-303, 307, 313, 314, 316 and 317.

In related embodiments, the isolated polynucleotide encodes an epitope of a polypeptide, wherein the polypeptide is encoded by a nucleotide sequence that: (a) hybridizes to a sequence recited in any one of SEQ ID NO: 1, 3-26, 28-77, 142, 143, 146-152, 154-166, 168-176, 178-192, 194-198, 200-204, 206, 207, 209-214, 216, 218, 219, 221-240, 243-245, 247, 250, 251, 253, 255, 257-266, 268, 269, 271-273, 275, 276, 278, 280, 281, 284, 288, 291-298, 301-303, 307, 313, 314, 316 and 317 under stringent conditions; and (b) is at least 80% identical to a sequence recited in any one of SEQ ID NO: 1, 3-26, 28-77, 142, 143, 146-152, 154-166, 168-176, 178-192, 194-198, 200-204, 206, 207, 209-214, 216, 218, 219, 221-240, 243-245, 247, 250, 251, 253, 255, 257-266, 268, 269, 271-273, 275, 276, 278, 280, 281, 284, 288, 291-298, 301-303, 307, 313, 314, 316 and 317.

In another embodiment, the present invention provides an isolated polynucleotide encoding an epitope of a polypeptide, the polypeptide being encoded by: (a) a nucleotide sequence transcribed from the sequence of SEQ ID NO: 141; or (b) a variant of said nucleotide sequence that contains one or more nucleotide substitutions, deletions, insertions and/or modifications at no more than 20% of the nucleotide positions, such that the antigenic and/or immunogenic properties of the polypeptide encoded by the nucleotide sequence are retained. Isolated DNA and RNA molecules comprising a nucleotide sequence complementary to a polynucleotide as described above are also provided.

In related aspects, the present invention provides recombinant expression vectors comprising a polynucleotide as described above and host cells transformed or transfected with such expression vectors.

In further aspects, polypeptides comprising an amino acid sequence encoded by a polynucleotide as described above, and monoclonal antibodies that bind to such polypeptides are provided. In certain embodiments, the inventive polypeptides comprise an amino acid sequence selected from the group consisting of SEQ ID NO: 299, 300, 304-306, 308 and 315, and variants thereof as defined below.

In yet another aspect, methods are provided for determining the presence of breast cancer in a patient. In one embodiment, the method comprises detecting, within a biological sample, a polypeptide as described above. In another embodiment, the method comprises detecting, within a biological sample, an RNA molecule encoding a polypeptide as described above. In yet another embodiment, the method comprises (a) intradermally injecting a patient with a polypeptide as described above; and (b) detecting an immune response on the patient's skin and therefrom detecting the presence of breast cancer in the patient. In further embodiments, the present invention provides methods for determining the presence of breast cancer in a patient as described above wherein the polypeptide is encoded by a nucleotide sequence selected from the group consisting of SEQ ID NO: 78-86, 144, 145, 153, 167, 177, 193, 199, 205, 208, 215, 217, 220, 241, 242, 246, 248, 249, 252, 256, 267, 270, 274, 277, 279, 282, 283, 285-287, 289, 290 and sequences that hybridize thereto under stringent conditions.

In a related aspect, diagnostic kits useful in the determination of breast cancer are provided. The diagnostic kits generally comprise either one or more monoclonal antibodies as described above, or one or more monoclonal antibodies that bind to a polypeptide encoded by a nucleotide sequence selected from the group consisting of sequences provided in SEQ ID NO: 78-86, 144, 145, 153, 167, 177, 193, 199, 205, 208, 215, 217, 220, 241, 242, and 246, 248, 249, 252, 256, 267, 270, 274, 277, 279, 282, 283, 285-287, 289, 290 and a detection reagent.

Diagnostic kits are also provided that comprise a first polymerase chain reaction primer and a second polymerase chain reaction primer, at least one of the primers being specific for a polynucleotide described herein. In one embodiment, at least one of the primers comprises at least about 10 contiguous nucleotides of a polynucleotide as described above, or a polynucleotide encoding a polypeptide encoded by a sequence selected from the group consisting of SEQ ID NO: 78-86, 144, 145, 153, 167, 177, 193, 199, 205, 208, 215, 217, 220, 241, 242, 246, 248, 249, 252, 256, 267, 270, 274, 277, 279, 282, 283, 285-287, 289 and 290.

Within another related aspect, the diagnostic kit comprises at least one oligonucleotide probe, the probe being specific for a polynucleotide described herein. In one embodiment, the probe comprises at least about 15 contiguous nucleotides of a polynucleotide as described above, or a polynucleotide selected from the group consisting of SEQ ID NO: 78-86, 144, 145, 153, 167, 177, 193, 199, 205, 208, 215, 217, 220, 241, 242, 246, 248, 249, 252, 256, 267, 270, 274, 277, 279, 282, 283, 285-287, 289 and 290.

In another related aspect, the present invention provides methods for monitoring the progression of breast cancer in a patient. In one embodiment, the method comprises: (a) detecting an amount, in a biological sample, of a polypeptide as described above at a first point in time; (b) repeating step (a) at a subsequent point in time; and (c) comparing the amounts of polypeptide detected in steps (a) and (b), and therefrom monitoring the progression of breast cancer in the patient. In another embodiment, the method comprises (a) detecting an amount, within a biological sample, of an RNA molecule encoding a polypeptide as described above at a first point in time; (b) repeating

step (a) at a subsequent point in time; and (c) comparing the amounts of RNA molecules detected in steps (a) and (b), and therefrom monitoring the progression of breast cancer in the patient. In yet other embodiments, the present invention provides methods for monitoring the progression of breast cancer in a patient as described above wherein the polypeptide is encoded by a nucleotide sequence selected from the group consisting of SEQ ID NO: 78-86, 144, 145, 153, 167, 177, 193, 199, 205, 208, 215, 217, 220, 241, 242, 246, 248, 249, 252, 256, 267, 270, 274, 277, 279, 282, 283, 285-287, 289, 290 and sequences that hybridize thereto under stringent conditions.

In still other aspects, pharmaceutical compositions, which comprise a polypeptide as described above in combination with a physiologically acceptable carrier, and vaccines, which comprise a polypeptide as described above in combination with an immunostimulant or adjuvant, are provided. In yet other aspects, the present invention provides pharmaceutical compositions and vaccines comprising a polypeptide encoded by a nucleotide sequence selected from the group consisting of SEQ ID NO: 78-86, 144, 145, 153, 167, 177, 193, 199, 205, 208, 215, 217, 220, 241, 242 and 246, 248, 249, 252, 256, 267, 270, 274, 277, 279, 282, 283, 285-287, 289, 290 and sequences that hybridize thereto under stringent conditions.

In related aspects, the present invention provides methods for inhibiting the development of breast cancer in a patient, comprising administering to a patient a pharmaceutical composition or vaccine as described above.

These and other aspects of the present invention will become apparent upon reference to the following detailed description and attached drawings. All references disclosed herein are hereby incorporated by reference in their entirety as if each was incorporated individually.

25 BRIEF DESCRIPTION OF THE DRAWINGS

Figure 1 shows the differential display PCR products, separated by gel electrophoresis, obtained from cDNA prepared from normal breast tissue (lanes 1 and 2) and from cDNA prepared from breast tumor tissue from the same patient (lanes 3 and 4). The arrow indicates the band corresponding to B18Ag1.

Figure 2 is a northern blot comparing the level of B18Ag1 mRNA in breast tumor tissue (lane 1) with the level in normal breast tissue.

Figure 3 shows the level of B18Ag1 mRNA in breast tumor tissue compared to that in various normal and non-breast tumor tissues as determined by RNase protection assays.

Figure 4 is a genomic clone map showing the location of additional retroviral sequences obtained from ends of XbaI restriction digests (provided in SEQ ID NO:3 - SEQ ID NO:10) relative to B18Ag1.

Figures 5A and 5B show the sequencing strategy, genomic organization and predicted open reading frame for the retroviral element containing B18Ag1.

Figure 6 shows the nucleotide sequence of the representative breast tumor-specific cDNA B18Ag1.

Figure 7 shows the nucleotide sequence of the representative breast tumor-specific cDNA B17Ag1.

Figure 8 shows the nucleotide sequence of the representative breast tumor-specific cDNA B17Ag2.

Figure 9 shows the nucleotide sequence of the representative breast tumor-specific cDNA B13Ag2a.

Figure 10 shows the nucleotide sequence of the representative breast tumor-specific cDNA B13Ag1b.

Figure 11 shows the nucleotide sequence of the representative breast tumor-specific cDNA B13Ag1a.

Figure 12 shows the nucleotide sequence of the representative breast tumor-specific cDNA B11Ag1.

Figure 13 shows the nucleotide sequence of the representative breast tumor-specific cDNA B3CA3c.

Figure 14 shows the nucleotide sequence of the representative breast tumor-specific cDNA B9CG1.

Figure 15 shows the nucleotide sequence of the representative breast tumor-specific cDNA B9CG3.

Figure 16 shows the nucleotide sequence of the representative breast tumor-specific cDNA B2CA2.

Figure 17 shows the nucleotide sequence of the representative breast tumor-specific cDNA B3CA1.

5 Figure 18 shows the nucleotide sequence of the representative breast tumor-specific cDNA B3CA2.

Figure 19 shows the nucleotide sequence of the representative breast tumor-specific cDNA B3CA3.

10 Figure 20 shows the nucleotide sequence of the representative breast tumor-specific cDNA B4CA1.

Figure 21A depicts RT-PCR analysis of breast tumor genes in breast tumor tissues (lanes 1-8) and normal breast tissues (lanes 9-13) and H₂O (lane 14).

15 Figure 21B depicts RT-PCR analysis of breast tumor genes in prostate tumors (lane 1, 2), colon tumors (lane 3), lung tumor (lane 4), normal prostate (lane 5), normal colon (lane 6), normal kidney (lane 7), normal liver (lane 8), normal lung (lane 9), normal ovary (lanes 10, 18), normal pancreases (lanes 11, 12), normal skeletal muscle (lane 13), normal skin (lane 14), normal stomach (lane 15), normal testes (lane 16), normal small intestine (lane 17), HBL-100 (lane 19), MCF-12A (lane 20), breast tumors (lanes 21-23), H₂O (lane 24), and colon tumor (lane 25).

20 Figure 22 shows the recognition of a B11Ag1 peptide (referred to as B11-8) by an anti-B11-8 CTL line.

Figure 23 shows the recognition of a cell line transduced with the antigen B11Ag1 by the B11-8 specific clone A1.

25 Figure 24 shows recognition of a lung adenocarcinoma line (LT-140-22) and a breast adenocarcinoma line (CAMA-1) by the B11-8 specific clone A1.

DETAILED DESCRIPTION OF THE INVENTION

As noted above, the present invention is generally directed to compositions and methods for the diagnosis, monitoring and therapy of breast cancer. The compositions described herein include polypeptides, polynucleotides and antibodies.

Polypeptides of the present invention generally comprise at least a portion of a protein that is expressed at a greater level in human breast tumor tissue than in normal breast tissue (i.e., the level of RNA encoding the polypeptide is at least 2-fold higher in tumor tissue). Such polypeptides are referred to herein as breast tumor-specific polypeptides, and cDNA molecules encoding such polypeptides are referred to as breast tumor-specific cDNAs. Polynucleotides of the subject invention generally comprise a DNA or RNA sequence that encodes all or a portion of a polypeptide as described above, or that is complementary to such a sequence. Antibodies are generally immune system proteins, or fragments thereof, that are capable of binding to a portion of a polypeptide as described above. Antibodies can be produced by cell culture techniques, including the generation of monoclonal antibodies as described herein, or via transfection of antibody genes into suitable bacterial or mammalian cell hosts, in order to allow for the production of recombinant antibodies.

Polypeptides within the scope of this invention include, but are not limited to, polypeptides (and epitopes thereof) encoded by a human endogenous retroviral sequence, such as the sequence designated B18Ag1 (Figure 5 and SEQ ID NO:1). Also, within the scope of the present invention are polypeptides encoded by other sequences within the retroviral genome containing B18Ag1 (SEQ ID NO: 141). Such sequences include, but are not limited to, the sequences recited in SEQ ID NO:3 - SEQ ID NO:10. B18Ag1 has homology to the *gag* p30 gene of the endogenous human retroviral element S71, as described in Werner et al., *Virology* 174:225-238 (1990) and also shows homology to about thirty other retroviral *gag* genes. As discussed in more detail below, the present invention also includes a number of additional breast tumor-specific polypeptides, such as those encoded by the nucleotide sequences recited in SEQ ID NO: 11-26, 28-77, 142, 143, 146-152, 154-166, 168-176, 178-192, 194-198, 200-204, 206, 207, 209-214, 216, 218, 219, 221-240, 243-245, 247, 250, 251, 253, 255, 257-266, 268, 269, 271-273, 275, 276, 278, 280, 281, 284, 288, 291-298, 301-303, 307, 313, 314, 316 and 317.

As used herein, the term "polypeptide" encompasses amino acid chains of any length, including full length proteins containing the sequences recited herein. A

polypeptide comprising an epitope of a protein containing a sequence as described herein may consist entirely of the epitope, or may contain additional sequences. The additional sequences may be derived from the native protein or may be heterologous, and such sequences may (but need not) possess immunogenic or antigenic properties.

5 An "epitope," as used herein is a portion of a polypeptide that is recognized (*i.e.*, specifically bound) by a B-cell and/or T-cell surface antigen receptor. Epitopes may generally be identified using well known techniques, such as those summarized in Paul, *Fundamental Immunology*, 3rd ed., 243-247 (Raven Press, 1993) and references cited therein. Such techniques include screening polypeptides derived
10 from the native polypeptide for the ability to react with antigen-specific antisera and/or T-cell lines or clones. An epitope of a polypeptide is a portion that reacts with such antisera and/or T-cells at a level that is similar to the reactivity of the full length polypeptide (*e.g.*, in an ELISA and/or T-cell reactivity assay). Such screens may generally be performed using methods well known to those of ordinary skill in the art,
15 such as those described in Harlow and Lane, *Antibodies: A Laboratory Manual*, Cold Spring Harbor Laboratory, 1988. B-cell and T-cell epitopes may also be predicted via computer analysis. Polypeptides comprising an epitope of a polypeptide that is preferentially expressed in a tumor tissue (with or without additional amino acid sequence) are within the scope of the present invention.

20 The term "polynucleotide(s)," as used herein, means a single or double-stranded polymer of deoxyribonucleotide or ribonucleotide bases and includes DNA and corresponding RNA molecules, including HnRNA and mRNA molecules, both sense and anti-sense strands, and comprehends cDNA, genomic DNA and recombinant DNA, as well as wholly or partially synthesized polynucleotides. An HnRNA molecule contains
25 introns and corresponds to a DNA molecule in a generally one-to-one manner. An mRNA molecule corresponds to an HnRNA and DNA molecule from which the introns have been excised. A polynucleotide may consist of an entire gene, or any portion thereof. Operable anti-sense polynucleotides may comprise a fragment of the corresponding polynucleotide, and the definition of "polynucleotide" therefore includes
30 all such operable anti-sense fragments.

The compositions and methods of the present invention also encompass variants of the above polypeptides and polynucleotides.

A polypeptide "variant," as used herein, is a polypeptide that differs from the recited polypeptide only in conservative substitutions and/or modifications, such that the antigenic properties of the polypeptide are retained. In a preferred embodiment, variant polypeptides differ from an identified sequence by substitution, deletion or addition of five amino acids or fewer. Such variants may generally be identified by modifying one of the above polypeptide sequences, and evaluating the antigenic properties of the modified polypeptide using, for example, the representative procedures described herein. Polypeptide variants preferably exhibit at least about 70%, more preferably at least about 90% and most preferably at least about 95% identity (determined as described below) to the identified polypeptides.

As used herein, a "conservative substitution" is one in which an amino acid is substituted for another amino acid that has similar properties, such that one skilled in the art of peptide chemistry would expect the secondary structure and hydrophobic nature of the polypeptide to be substantially unchanged. In general, the following groups of amino acids represent conservative changes: (1) ala, pro, gly, glu, asp, gln, asn, ser, thr; (2) cys, ser, tyr, thr; (3) val, ile, leu, met, ala, phe; (4) lys, arg, his; and (5) phe, tyr, trp, his.

Variants may also, or alternatively, contain other modifications, including the deletion or addition of amino acids that have minimal influence on the antigenic properties, secondary structure and hydrophobic nature of the polypeptide. For example, a polypeptide may be conjugated to a signal (or leader) sequence at the N-terminal end of the protein which co-translationally or post-translationally directs transfer of the protein. The polypeptide may also be conjugated to a linker or other sequence for ease of synthesis, purification or identification of the polypeptide (e.g., poly-His), or to enhance binding of the polypeptide to a solid support. For example, a polypeptide may be conjugated to an immunoglobulin Fc region.

A nucleotide "variant" is a sequence that differs from the recited nucleotide sequence in having one or more nucleotide deletions, substitutions or

additions. Such modifications may be readily introduced using standard mutagenesis techniques, such as oligonucleotide-directed site-specific mutagenesis as taught, for example, by Adelman et al. (*DNA*, 2:183, 1983). Nucleotide variants may be naturally occurring allelic variants, or non-naturally occurring variants. Variant nucleotide sequences preferably exhibit at least about 70%, more preferably at least about 80% and most preferably at least about 90% identity (determined as described below) to the recited sequence.

The breast tumor antigens provided by the present invention include variants that are encoded by DNA sequences which are substantially homologous to one or more of the DNA sequences specifically recited herein. "Substantial homology," as used herein, refers to DNA sequences that are capable of hybridizing under moderately stringent conditions. Suitable moderately stringent conditions include prewashing in a solution of 5X SSC, 0.5% SDS, 1.0 mM EDTA (pH 8.0); hybridizing at 50°C-65°C, 5X SSC; overnight or, in the event of cross-species homology, at 45°C with 0.5X SSC; followed by washing twice at 65°C for 20 minutes with each of 2X, 0.5X and 0.2X SSC containing 0.1% SDS. Such hybridizing DNA sequences are also within the scope of this invention, as are nucleotide sequences that, due to code degeneracy, encode an immunogenic polypeptide that is encoded by a hybridizing DNA sequence.

Two nucleotide or polypeptide sequences are said to be "identical" if the sequence of nucleotides or amino acid residues in the two sequences is the same when aligned for maximum correspondence as described below. Comparisons between two sequences are typically performed by comparing the sequences over a comparison window to identify and compare local regions of sequence similarity. A "comparison window" as used herein, refers to a segment of at least about 20 contiguous positions, usually 30 to about 75, 40 to about 50, in which a sequence may be compared to a reference sequence of the same number of contiguous positions after the two sequences are optimally aligned.

Optimal alignment of sequences for comparison may be conducted using the Megalign program in the Lasergene suite of bioinformatics software (DNASTAR, Inc., Madison, WI), using default parameters. This program embodies several alignment

- schemes described in the following references: Dayhoff, M.O. (1978) A model of evolutionary change in proteins - Matrices for detecting distant relationships. In Dayhoff, M.O. (ed.) Atlas of Protein Sequence and Structure, National Biomedical Research Foundation, Washington DC Vol. 5, Suppl. 3, pp. 345-358; Hein J. (1990)
- 5 Unified Approach to Alignment and Phylogenies pp. 626-645 *Methods in Enzymology* vol. 183, Academic Press, Inc., San Diego, CA; Higgins, D.G. and Sharp, P.M. (1989) Fast and sensitive multiple sequence alignments on a microcomputer *CABIOS* 5:151-153; Myers, E.W. and Muller W. (1988) Optimal alignments in linear space *CABIOS* 4:11-17; Robinson, E.D. (1971) *Comb. Theor* 11:105; Santou, N. Nes, M. (1987) The
 - 10 neighbor joining method. A new method for reconstructing phylogenetic trees *Mol. Biol. Evol.* 4:406-425; Sneath, P.H.A. and Sokal, R.R. (1973) *Numerical Taxonomy - the Principles and Practice of Numerical Taxonomy*, Freeman Press, San Francisco, CA; Wilbur, W.J. and Lipman, D.J. (1983) Rapid similarity searches of nucleic acid and protein data banks *Proc. Natl. Acad., Sci. USA* 80:726-730.

15 Preferably, the "percentage of sequence identity" is determined by comparing two optimally aligned sequences over a window of comparison of at least 20 positions, wherein the portion of the polynucleotide sequence in the comparison window may comprise additions or deletions (i.e. gaps) of 20 percent or less, usually 5 to 15 percent, or 10 to 12 percent, as compared to the reference sequences (which does not comprise additions or deletions) for optimal alignment of the two sequences. The percentage is calculated by determining the number of positions at which the identical nucleic acid bases or amino acid residue occurs in both sequences to yield the number of matched positions, dividing the number of matched positions by the total number of positions in the reference sequence (i.e. the window size) and multiplying the

25 results by 100 to yield the percentage of sequence identity. In general, polynucleotides encoding all or a portion of the polypeptides described herein may be prepared using any of several techniques. For example, cDNA molecules encoding such polypeptides may be cloned on the basis of the breast tumor-specific expression of the corresponding mRNAs, using differential display PCR. This technique compares the amplified

30 products from RNA template prepared from normal and breast tumor tissue. cDNA may

be prepared by reverse transcription of RNA using a (dT)₁₂AG primer. Following amplification of the cDNA using a random primer, a band corresponding to an amplified product specific to the tumor RNA may be cut out from a silver stained gel and subcloned into a suitable vector (e.g., the T-vector, Novagen, Madison, WI).

- 5 Polynucleotides encoding all or a portion of the breast tumor-specific polypeptides disclosed herein may be amplified from cDNA prepared as described above using the random primers shown in SEQ ID NO.:87-125.

Alternatively, a polynucleotide encoding a polypeptide as described herein (or a portion thereof) may be amplified from human genomic DNA, or from breast
10 tumor cDNA, via polymerase chain reaction. For this approach, B18Ag1 sequence-specific primers may be designed based on the sequence provided in SEQ ID NO:1, and may be purchased or synthesized. One suitable primer pair for amplification from breast tumor cDNA is (5'ATG GCT ATT TTC GGG GGC TGA CA) (SEQ ID NO:126) and (5'CCG GTA TCT CCT CGT GGG TAT T) (SEQ ID NO:127). An amplified portion of
15 B18Ag1 may then be used to isolate the full length gene from a human genomic DNA library or from a breast tumor cDNA library, using well known techniques, such as those described in Sambrook et al., *Molecular Cloning: A Laboratory Manual*, Cold Spring Harbor Laboratories, Cold Spring Harbor, NY (1989). Other sequences within the retroviral genome of which B18Ag1 is a part may be similarly prepared by screening
20 human genomic libraries using B18Ag1-specific sequences as probes. Nucleotides translated into protein from the retroviral genome shown in SEQ ID NO: 141 may then be determined by cloning the corresponding cDNAs, predicting the open reading frames and cloning the appropriate cDNAs into a vector containing a viral promoter, such as T7. The resulting constructs can be employed in a translation reaction, using techniques
25 known to those of skill in the art, to identify nucleotide sequences which result in expressed protein. Similarly, primers specific for the remaining breast tumor-specific polypeptides described herein may be designed based on the nucleotide sequences provided in SEQ ID NO:11-86, 142-298, 301-303, 307, 313, 314, 316 and 317.

Recombinant polypeptides encoded by the DNA sequences described
30 above may be readily prepared from the DNA sequences. For example, supernatants

from suitable host/vector systems which secrete recombinant protein or polypeptide into culture media may be first concentrated using a commercially available filter. Following concentration, the concentrate may be applied to a suitable purification matrix such as an affinity matrix or an ion exchange resin. Finally, one or more reverse phase HPLC steps can be employed to further purify a recombinant polypeptide.

In general, any of a variety of expression vectors known to those of ordinary skill in the art may be employed to express recombinant polypeptides of this invention. Expression may be achieved in any appropriate host cell that has been transformed or transfected with an expression vector containing a polynucleotide that encodes a recombinant polypeptide. Suitable host cells include prokaryotes, yeast and higher eukaryotic cells. Preferably, the host cells employed are *E. coli*, yeast or a mammalian cell line such as COS or CHO.

Such techniques may also be used to prepare polypeptides comprising epitopes or variants of the native polypeptides. For example, variants of a native polypeptide may generally be prepared using standard mutagenesis techniques, such as oligonucleotide-directed site-specific mutagenesis, and sections of the DNA sequence may be removed to permit preparation of truncated polypeptides. Portions and other variants having fewer than about 100 amino acids, and generally fewer than about 50 amino acids, may also be generated by synthetic means, using techniques well known to those of ordinary skill in the art. For example, such polypeptides may be synthesized using any of the commercially available solid-phase techniques, such as the Merrifield solid-phase synthesis method, where amino acids are sequentially added to a growing amino acid chain. See Merrifield, *J. Am. Chem. Soc.* 85:2149-2146 (1963). Equipment for automated synthesis of polypeptides is commercially available from suppliers such as Perkin Elmer/Applied BioSystems Division, Foster City, CA, and may be operated according to the manufacturer's instructions.

In specific embodiments, polypeptides of the present invention encompass amino acid sequences encoded by a polynucleotide having a sequence recited in any one of SEQ ID NO:1, 3-26, 28-77, 142, 143, 146-152, 154-166, 168-176, 178-192, 194-198, 200-204, 206, 207, 209-214, 216, 218, 219, 221-240, 243-245, 247, 250, 251, 253, 255,

257-266, 268, 269, 271-273, 275, 276, 278, 280, 281, 284, 288, 291-298, 301-303, 307, 313, 314, 316 and 317, and variants of such polypeptides. Polypeptides within the scope of the present invention also include polypeptides (and epitopes thereof) encoded by DNA sequences that hybridize to a sequence recited in any one of SEQ ID NO:1, 3-26, 28-77, 142, 143, 146-152, 154-166, 168-176, 178-192, 194-198, 200-204, 206, 207, 209-214, 216, 218, 219, 221-240, 243-245, 247, 250, 251, 253, 255, 257-266, 268, 269, 271-273, 275, 276, 278, 280, 281, 284, 288, 291-298, 301-303, 307, 313, 314, 316 and 317 under stringent conditions, wherein the DNA sequences are at least 80% identical in overall sequence to a recited sequence and wherein RNA corresponding to the nucleotide sequence is expressed at a greater level in human breast tumor tissue than in normal breast tissue. As used herein, "stringent conditions" refers to prewashing in a solution of 6X SSC, 0.2% SDS; hybridizing at 65°C, 6X SSC, 0.2% SDS overnight; followed by two washes of 30 minutes each in 1X SSC, 0.1% SDS at 65°C and two washes of 30 minutes each in 0.2 X SSC, 0.1% SDS at 65°C. Polynucleotides according to the present invention include molecules that encode any of the above polypeptides.

In another aspect of the present invention, antibodies are provided. Such antibodies may be prepared by any of a variety of techniques known to those of ordinary skill in the art. See, e.g., Harlow and Lane, *Antibodies: A Laboratory Manual*, Cold Spring Harbor Laboratory, 1988. In one such technique, an immunogen comprising the polypeptide is initially injected into any of a wide variety of mammals (e.g., mice, rats, rabbits, sheep or goats). In this step, the polypeptides of this invention may serve as the immunogen without modification. Alternatively, particularly for relatively short polypeptides, a superior immune response may be elicited if the polypeptide is joined to a carrier protein, such as bovine serum albumin or keyhole limpet hemocyanin. The immunogen is injected into the animal host, preferably according to a predetermined schedule incorporating one or more booster immunizations, and the animals are bled periodically. Polyclonal antibodies specific for the polypeptide may then be purified from such antisera by, for example, affinity chromatography using the polypeptide coupled to a suitable solid support.

Monoclonal antibodies specific for the antigenic polypeptide of interest may be prepared, for example, using the technique of Kohler and Milstein, *Eur. J. Immunol.* 6:511-519 (1976), and improvements thereto. Briefly, these methods involve the preparation of immortal cell lines capable of producing antibodies having the desired specificity (i.e., reactivity with the polypeptide of interest). Such cell lines may be produced, for example, from spleen cells obtained from an animal immunized as described above. The spleen cells are then immortalized by, for example, fusion with a myeloma cell fusion partner, preferably one that is syngeneic with the immunized animal. A variety of fusion techniques may be employed. For example, the spleen cells and myeloma cells may be combined with a nonionic detergent for a few minutes and then plated at low density on a selective medium that supports the growth of hybrid cells, but not myeloma cells. A preferred selection technique uses HAT (hypoxanthine, aminopterin, thymidine) selection. After a sufficient time, usually about 1 to 2 weeks, colonies of hybrids are observed. Single colonies are selected and their culture supernatants tested for binding activity against the polypeptide. Hybridomas having high reactivity and specificity are preferred.

Monoclonal antibodies may be isolated from the supernatants of growing hybridoma colonies. In addition, various techniques may be employed to enhance the yield, such as injection of the hybridoma cell line into the peritoneal cavity of a suitable vertebrate host, such as a mouse. Monoclonal antibodies may then be harvested from the ascites fluid or the blood. Contaminants may be removed from the antibodies by conventional techniques, such as chromatography, gel filtration, precipitation, and extraction. The polypeptides of this invention may be used in the purification process in, for example, an affinity chromatography step.

Antibodies may be used, for example, in methods for detecting breast cancer in a patient. Such methods involve using an antibody to detect the presence or absence of a breast tumor-specific polypeptide as described herein in a suitable biological sample. As used herein, suitable biological samples include tumor or normal tissue biopsy, mastectomy, blood, lymph node, serum or urine samples, or other tissue, homogenate, or extract thereof obtained from a patient.

There are a variety of assay formats known to those of ordinary skill in the art for using an antibody to detect polypeptide markers in a sample. See, e.g., Harlow and Lane, *Antibodies: A Laboratory Manual*, Cold Spring Harbor Laboratory, 1988. For example, the assay may be performed in a Western blot format, wherein a protein preparation from the biological sample is submitted to gel electrophoresis, transferred to a suitable membrane and allowed to react with the antibody. The presence of the antibody on the membrane may then be detected using a suitable detection reagent, as described below.

In another embodiment, the assay involves the use of antibody immobilized on a solid support to bind to the polypeptide and remove it from the remainder of the sample. The bound polypeptide may then be detected using a second antibody or reagent that contains a reporter group. Alternatively, a competitive assay may be utilized, in which a polypeptide is labeled with a reporter group and allowed to bind to the immobilized antibody after incubation of the antibody with the sample. The extent to which components of the sample inhibit the binding of the labeled polypeptide to the antibody is indicative of the reactivity of the sample with the immobilized antibody, and as a result, indicative of the concentration of polypeptide in the sample.

The solid support may be any material known to those of ordinary skill in the art to which the antibody may be attached. For example, the solid support may be a test well in a microtiter plate or a nitrocellulose filter or other suitable membrane. Alternatively, the support may be a bead or disc, such as glass, fiberglass, latex or a plastic material such as polystyrene or polyvinylchloride. The support may also be a magnetic particle or a fiber optic sensor, such as those disclosed, for example, in U.S. Patent No. 5,359,681.

The antibody may be immobilized on the solid support using a variety of techniques known to those in the art, which are amply described in the patent and scientific literature. In the context of the present invention, the term "immobilization" refers to both noncovalent association, such as adsorption, and covalent attachment (which may be a direct linkage between the antigen and functional groups on the support or may be a linkage by way of a cross-linking agent). Immobilization by adsorption to a

well in a microtiter plate or to a membrane is preferred. In such cases, adsorption may be achieved by contacting the antibody, in a suitable buffer, with the solid support for a suitable amount of time. The contact time varies with temperature, but is typically between about 1 hour and 1 day. In general, contacting a well of a plastic microtiter plate (such as polystyrene or polyvinylchloride) with an amount of antibody ranging from about 10 ng to about 1 µg, and preferably about 100-200 ng, is sufficient to immobilize an adequate amount of polypeptide.

Covalent attachment of antibody to a solid support may also generally be achieved by first reacting the support with a bifunctional reagent that will react with both the support and a functional group, such as a hydroxyl or amino group, on the antibody. For example, the antibody may be covalently attached to supports having an appropriate polymer coating using benzoquinone or by condensation of an aldehyde group on the support with an amine and an active hydrogen on the binding partner (*see, e.g.,* Pierce Immunotechnology Catalog and Handbook (1991) at A12-A13).

In certain embodiments, the assay for detection of polypeptide in a sample is a two-antibody sandwich assay. This assay may be performed by first contacting an antibody that has been immobilized on a solid support, commonly the well of a microtiter plate, with the biological sample, such that the polypeptide within the sample are allowed to bind to the immobilized antibody. Unbound sample is then removed from the immobilized polypeptide-antibody complexes and a second antibody (containing a reporter group) capable of binding to a different site on the polypeptide is added. The amount of second antibody that remains bound to the solid support is then determined using a method appropriate for the specific reporter group.

More specifically, once the antibody is immobilized on the support as described above, the remaining protein-binding sites on the support are typically blocked.

Any suitable blocking agent known to those of ordinary skill in the art, such as bovine serum albumin or Tween 20™ (Sigma Chemical Co., St. Louis, MO). The immobilized antibody is then incubated with the sample, and polypeptide is allowed to bind to the antibody. The sample may be diluted with a suitable diluent, such as phosphate-buffered saline (PBS) prior to incubation. In general, an appropriate contact time (*i.e.,* incubation

time) is that period of time that is sufficient to detect the presence of polypeptide within a sample obtained from an individual with breast cancer. Preferably, the contact time is sufficient to achieve a level of binding that is at least 95% of that achieved at equilibrium between bound and unbound polypeptide. Those of ordinary skill in the art will recognize that the time necessary to achieve equilibrium may be readily determined by assaying the level of binding that occurs over a period of time. At room temperature, an incubation time of about 30 minutes is generally sufficient.

Unbound sample may then be removed by washing the solid support with an appropriate buffer, such as PBS containing 0.1% Tween 20™. The second antibody, which contains a reporter group, may then be added to the solid support. Preferred reporter groups include enzymes (such as horseradish peroxidase), substrates, cofactors, inhibitors, dyes, radionuclides, luminescent groups, fluorescent groups and biotin. The conjugation of antibody to reporter group may be achieved using standard methods known to those of ordinary skill in the art.

The second antibody is then incubated with the immobilized antibody-polypeptide complex for an amount of time sufficient to detect the bound polypeptide. An appropriate amount of time may generally be determined by assaying the level of binding that occurs over a period of time. Unbound second antibody is then removed and bound second antibody is detected using the reporter group. The method employed for detecting the reporter group depends upon the nature of the reporter group. For radioactive groups, scintillation counting or autoradiographic methods are generally appropriate. Spectroscopic methods may be used to detect dyes, luminescent groups and fluorescent groups. Biotin may be detected using avidin, coupled to a different reporter group (commonly a radioactive or fluorescent group or an enzyme). Enzyme reporter groups may generally be detected by the addition of substrate (generally for a specific period of time), followed by spectroscopic or other analysis of the reaction products.

To determine the presence or absence of breast cancer, the signal detected from the reporter group that remains bound to the solid support is generally compared to a signal that corresponds to a predetermined cut-off value established from non-tumor tissue. In one preferred embodiment, the cut-off value is the average mean signal

obtained when the immobilized antibody is incubated with samples from patients without breast cancer. In general, a sample generating a signal that is three standard deviations above the predetermined cut-off value may be considered positive for breast cancer. In an alternate preferred embodiment, the cut-off value is determined using a Receiver Operator Curve, according to the method of Sackett et al., *Clinical Epidemiology: A Basic Science for Clinical Medicine*, p. 106-7 (Little Brown and Co., 1985). Briefly, in this embodiment, the cut-off value may be determined from a plot of pairs of true positive rates (i.e., sensitivity) and false positive rates (100%-specificity) that correspond to each possible cut-off value for the diagnostic test result. The cut-off value on the plot that is the closest to the upper left-hand corner (i.e., the value that encloses the largest area) is the most accurate cut-off value, and a sample generating a signal that is higher than the cut-off value determined by this method may be considered positive. Alternatively, the cut-off value may be shifted to the left along the plot, to minimize the false positive rate, or to the right, to minimize the false negative rate. In general, a sample generating a signal that is higher than the cut-off value determined by this method is considered positive for breast cancer.

In a related embodiment, the assay is performed in a flow-through or strip test format, wherein the antibody is immobilized on a membrane, such as nitrocellulose. In the flow-through test, the polypeptide within the sample bind to the immobilized antibody as the sample passes through the membrane. A second, labeled antibody then binds to the antibody-polypeptide complex as a solution containing the second antibody flows through the membrane. The detection of bound second antibody may then be performed as described above. In the strip test format, one end of the membrane to which antibody is bound is immersed in a solution containing the sample. The sample migrates along the membrane through a region containing second antibody and to the area of immobilized antibody. Concentration of second antibody at the area of immobilized antibody indicates the presence of breast cancer. Typically, the concentration of second antibody at that site generates a pattern, such as a line, that can be read visually. The absence of such a pattern indicates a negative result. In general, the amount of antibody immobilized on the membrane is selected to generate a visually

discernible pattern when the biological sample contains a level of polypeptide that would be sufficient to generate a positive signal in the two-antibody sandwich assay, in the format discussed above. Preferably, the amount of antibody immobilized on the membrane ranges from about 25 ng to about 1 μ g, and more preferably from about 50 ng to about 1 μ g. Such tests can typically be performed with a very small amount of biological sample.

The presence or absence of breast cancer in a patient may also be determined by evaluating the level of mRNA encoding a breast tumor-specific polypeptide as described herein within the biological sample (e.g., a biopsy, mastectomy and/or blood sample from a patient) relative to a predetermined cut-off value. Such an evaluation may be achieved using any of a variety of methods known to those of ordinary skill in the art such as, for example, *in situ* hybridization and amplification by polymerase chain reaction.

For example, polymerase chain reaction may be used to amplify sequences from cDNA prepared from RNA that is isolated from one of the above biological samples. Sequence-specific primers for use in such amplification may be designed based on the sequences provided in any one of SEQ ID NO: 1, 11-86, 142-298 301-303, 307, 313, 314, 316 and 317, and may be purchased or synthesized. In the case of B18Ag1, as noted herein, one suitable primer pair is B18Ag1-2 (5'ATG GCT ATT TTC GGG GGC TGA CA) (SEQ ID NO:126) and B18Ag1-3 (5'CCG GTA TCT CCT CGT GGG TAT T) (SEQ ID NO:127). The PCR reaction products may then be separated by gel electrophoresis and visualized according to methods well known to those of ordinary skill in the art. Amplification is typically performed on samples obtained from matched pairs of tissue (tumor and non-tumor tissue from the same individual) or from unmatched pairs of tissue (tumor and non-tumor tissue from different individuals). The amplification reaction is preferably performed on several dilutions of cDNA spanning two orders of magnitude. A two-fold or greater increase in expression in several dilutions of the tumor sample as compared to the same dilution of the non-tumor sample is considered positive.

As used herein, the term "primer/probe specific for a polynucleotide" means an oligonucleotide sequence that has at least about 80% identity, preferably at least about 90%, and more preferably at least about 95%, identity to the polynucleotide in question, or an oligonucleotide sequence that is anti-sense to a sequence that has at least about 80% identity, preferably at least about 90% and more preferably at least about 95%, identity to the polynucleotide in question. Primers and/or probes which may be usefully employed in the inventive diagnostic methods preferably have at least about 10-40 nucleotides. In a preferred embodiment, the polymerase chain reaction primers comprise at least about 10 contiguous nucleotides of a polynucleotide that encodes one of the polypeptides disclosed herein or that is anti-sense to a sequence that encodes one of the polypeptides disclosed herein. Preferably, oligonucleotide probes for use in the inventive diagnostic methods comprise at least about 15 contiguous oligonucleotides of a polynucleotide that encodes one of the polypeptides disclosed herein or that is anti-sense to a sequence that encodes one of the polypeptides disclosed herein. Techniques for both PCR based assays and *in situ* hybridization assays are well known in the art.

Conventional RT-PCR protocols using agarose and ethidium bromide staining, while important in defining gene specificity, do not lend themselves to diagnostic kit development because of the time and effort required in making them quantitative (i.e., construction of saturation and/or titration curves), and their sample throughput. This problem is overcome by the development of procedures such as real time RT-PCR which allows for assays to be performed in single tubes, and in turn can be modified for use in 96 well plate formats. Instrumentation to perform such methodologies are available from Perkin Elmer/Applied Biosystems Division. Alternatively, other high throughput assays using labeled probes (e.g., digoxigenin) in combination with labeled (e.g., enzyme fluorescent, radioactive) antibodies to such probes can also be used in the development of 96 well plate assays.

In yet another method for determining the presence or absence of breast cancer in a patient, one or more of the breast tumor-specific polypeptides described may be used in a skin test. As used herein, a "skin test" is any assay performed directly on a patient in which a delayed-type hypersensitivity (DTH) reaction (such as swelling,

reddening or dermatitis) is measured following intradermal injection of one or more polypeptides as described above. Such injection may be achieved using any suitable device sufficient to contact the polypeptide or polypeptides with dermal cells of the patient, such as a tuberculin syringe or 1 mL syringe. Preferably, the reaction is measured at least 48 hours after injection, more preferably 48-72 hours.

The DTH reaction is a cell-mediated immune response, which is greater in patients that have been exposed previously to a test antigen (*i.e.*, an immunogenic portion of a polypeptide employed, or a variant thereof). The response may be measured visually, using a ruler. In general, a response that is greater than about 0.5 cm in diameter, preferably greater than about 5.0 cm in diameter, is a positive response, indicative of breast cancer.

The breast tumor-specific polypeptides described herein are preferably formulated, for use in a skin test, as pharmaceutical compositions containing at least one polypeptide and a physiologically acceptable carrier, such as water, saline, alcohol, or a buffer. Such compositions typically contain one or more of the above polypeptides in an amount ranging from about 1 μ g to 100 μ g, preferably from about 10 μ g to 50 μ g in a volume of 0.1 mL. Preferably, the carrier employed in such pharmaceutical compositions is a saline solution with appropriate preservatives, such as phenol and/or Tween 80™.

In other aspects of the present invention, the progression and/or response to treatment of a breast cancer may be monitored by performing any of the above assays over a period of time, and evaluating the change in the level of the response (*i.e.*, the amount of polypeptide or mRNA detected or, in the case of a skin test, the extent of the immune response detected). For example, the assays may be performed every month to every other month for a period of 1 to 2 years. In general, breast cancer is progressing in those patients in whom the level of the response increases over time. In contrast, breast cancer is not progressing when the signal detected either remains constant or decreases with time.

In further aspects of the present invention, the compounds described herein may be used for the immunotherapy of breast cancer. In these aspects, the

compounds (which may be polypeptides, antibodies or polynucleotides) are preferably incorporated into pharmaceutical compositions or vaccines. Pharmaceutical compositions comprise one or more such compounds and a physiologically acceptable carrier. Vaccines may comprise one or more such compounds in combination with an immunostimulant, such as an adjuvant or a liposome (into which the compound is incorporated). An immunostimulant may be any substance that enhances or potentiates an immune response (antibody and/or cell-mediated) to an exogenous antigen. Examples of immunostimulants include adjuvants, biodegradable microspheres (e.g., polylactic galactide) and liposomes (into which the compound is incorporated; see e.g., Fullerton, U.S. Patent No. 4,235,877). Vaccine preparation is generally described in, for example, M.F. Powell and M.J. Newman, eds., "Vaccine Design (the subunit and adjuvant approach)," Plenum Press (NY, 1995). Pharmaceutical compositions and vaccines within the scope of the present invention may also contain other compounds, which may be biologically active or inactive. For example, one or more immunogenic portions of other tumor antigens may be present, either incorporated into a fusion polypeptide or as a separate compound, within the composition or vaccine.

Alternatively, a vaccine may contain DNA encoding one or more of the polypeptides as described above, such that the polypeptide is generated *in situ*. In such vaccines, the DNA may be present within any of a variety of delivery systems known to those of ordinary skill in the art, including nucleic acid expression systems, bacteria and viral expression systems. Appropriate nucleic acid expression systems contain the necessary DNA sequences for expression in the patient (such as a suitable promoter and terminating signal). Bacterial delivery systems involve the administration of a bacterium (such as *Bacillus-Calmette-Guerrin*) that expresses an immunogenic portion of the polypeptide on its cell surface. In a preferred embodiment, the DNA may be introduced using a viral expression system (e.g., vaccinia or other pox virus, retrovirus, or adenovirus), which may involve the use of a non-pathogenic (defective), replication competent virus. Techniques for incorporating DNA into such expression systems are well known to those of ordinary skill in the art. The DNA may also be "naked," as described, for example, in Ulmer et al., *Science* 259:1745-1749 (1993); and reviewed by

Cohen, *Science* 259:1691-1692 (1993). The uptake of naked DNA may be increased by coating the DNA onto biodegradable beads, which are efficiently transported into the cells.

While any suitable carrier known to those of ordinary skill in the art may be employed in the pharmaceutical compositions of this invention, the type of carrier will vary depending on the mode of administration. For parenteral administration, such as subcutaneous injection, the carrier preferably comprises water, saline, alcohol, a fat, a wax or a buffer. For oral administration, any of the above carriers or a solid carrier, such as mannitol, lactose, starch, magnesium stearate, sodium saccharine, talcum, cellulose, glucose, sucrose, and magnesium carbonate, may be employed. Biodegradable microspheres (e.g., polylactate polyglycolate) may also be employed as carriers for the pharmaceutical compositions of this invention.

Any of a variety of immunostimulants may be employed in the vaccines of this invention. For example, an adjuvant may be included. Most adjuvants contain a substance designed to protect the antigen from rapid catabolism, such as aluminum hydroxide or mineral oil, and a stimulator of immune responses, such as lipid A, *Bordetella pertussis* or *Mycobacterium tuberculosis* derived proteins. Suitable adjuvants are commercially available as, for example, Freund's Incomplete Adjuvant and Complete Adjuvant (Difco Laboratories, Detroit, MI); Merck Adjuvant 65 (Merck and Company, Inc., Rahway, NJ); AS-2 (SmithKline Beecham, Philadelphia, PA); aluminum salts such as aluminum hydroxide gel (alum) or aluminum phosphate; salts of calcium, iron or zinc; an insoluble suspension of acylated tyrosine; acylated sugars; cationically or anionically derivatized polysaccharides; polyphosphazenes; biodegradable microspheres; monophosphoryl lipid A and quil A. Cytokines, such as GM-CSF or interleukin-2, -7, or -12, may also be used as adjuvants.

Within the vaccines provided herein, the adjuvant composition is preferably designed to induce an immune response predominantly of the Th1 type. High levels of Th1-type cytokines (e.g., IFN- γ , TNF α , IL-2 and IL-12) tend to favor the induction of cell mediated immune responses to an administered antigen. In contrast, high levels of Th2-type cytokines (e.g., IL-4, IL-5, IL-6 and IL-10) tend to favor the

induction of humoral immune responses. Following application of a vaccine as provided herein, a patient will support an immune response that includes Th1- and Th2-type responses. Within a preferred embodiment, in which a response is predominantly Th1-type, the level of Th1-type cytokines will increase to a greater extent than the level of Th2-type cytokines. The levels of these cytokines may be readily assessed using standard assays. For a review of the families of cytokines, see Mosmann and Coffman, *Ann. Rev. Immunol.* 7:145-173, 1989.

Preferred adjuvants for use in eliciting a predominantly Th1-type response include, for example, a combination of monophosphoryl lipid A, preferably 3-de-O-acylated monophosphoryl lipid A (3D-MPL), together with an aluminum salt. MPL adjuvants are available from Corixa Corporation (Seattle, WA; see US Patent Nos. 4,436,727; 4,877,611; 4,866,034 and 4,912,094). CpG-containing oligonucleotides (in which the CpG dinucleotide is unmethylated) also induce a predominantly Th1 response. Such oligonucleotides are well known and are described, for example, in WO 96/02555 and WO 99/33488. Immunostimulatory DNA sequences are also described, for example, by Sato et al., *Science* 273:352, 1996. Another preferred adjuvant is a saponin, preferably QS21 (Aquila Biopharmaceuticals Inc., Framingham, MA), which may be used alone or in combination with other adjuvants. For example, an enhanced system involves the combination of a monophosphoryl lipid A and saponin derivative, such as the combination of QS21 and 3D-MPL as described in WO 94/00153, or a less reactogenic composition where the QS21 is quenched with cholesterol, as described in WO 96/33739. Other preferred formulations comprise an oil-in-water emulsion and tocopherol. A particularly potent adjuvant formulation involving QS21, 3D-MPL and tocopherol in an oil-in-water emulsion is described in WO 95/17210.

Other preferred adjuvants include Montanide ISA 720 (Seppic, France), SAF (Chiron, California, United States), ISCOMS (CSL), MF-59 (Chiron), the SBAS series of adjuvants (e.g., SBAS-2 or SBAS-4, available from SmithKline Beecham, Rixensart, Belgium), Detox (Ribi ImmunoChem Research Inc., Hamilton, MT), RC-529 (Ribi ImmunoChem Research Inc., Hamilton, MT) and Aminoalkyl glucosaminide 4-phosphates (AGPs).

Any vaccine provided herein may be prepared using well known methods that result in a combination of antigen, immunostimulant and a suitable carrier or excipient. The compositions described herein may be administered as part of a sustained release formulation (*i.e.*, a formulation such as a capsule, sponge or gel (composed of polysaccharides, for example) that effects a slow release of compound following administration). Such formulations may generally be prepared using well known technology (*see, e.g.*, Coombes et al., *Vaccine* 14:1429-1438, 1996) and administered by, for example, oral, rectal or subcutaneous implantation, or by implantation at the desired target site. Sustained-release formulations may contain a polypeptide, polynucleotide or antibody dispersed in a carrier matrix and/or contained within a reservoir surrounded by a rate controlling membrane.

Carriers for use within such formulations are biocompatible, and may also be biodegradable; preferably the formulation provides a relatively constant level of active component release. Such carriers include microparticles of poly(lactide-co-glycolide), as well as polyacrylate, latex, starch, cellulose and dextran. Other delayed-release carriers include supramolecular biovectors, which comprise a non-liquid hydrophilic core (*e.g.*, a cross-linked polysaccharide or oligosaccharide) and, optionally, an external layer comprising an amphiphilic compound, such as a phospholipid (*see e.g.*, U.S. Patent No. 5,151,254 and PCT applications WO 94/29078, WO/94/23701 and WO 96/06638). The amount of active compound contained within a sustained release formulation depends upon the site of implantation, the rate and expected duration of release and the nature of the condition to be treated or prevented.

Any of a variety of delivery vehicles may be employed within pharmaceutical compositions and vaccines to facilitate production of an antigen-specific immune response that targets tumor cells. Delivery vehicles include antigen presenting cells (APCs), such as dendritic cells, macrophages, B cells, monocytes and other cells that may be engineered to be efficient APCs. Such cells may, but need not, be genetically modified to increase the capacity for presenting the antigen, to improve activation and/or maintenance of the T cell response, to have anti-tumor effects *per se* and/or to be immunologically compatible with the receiver (*i.e.*, matched HLA

haplotype). APCs may generally be isolated from any of a variety of biological fluids and organs, including tumor and peritumoral tissues, and may be autologous, allogeneic, syngeneic or xenogeneic cells.

Certain preferred embodiments of the present invention use dendritic cells or progenitors thereof as antigen-presenting cells. Dendritic cells are highly potent APCs (Banchereau and Steinman, *Nature* 392:245-251, 1998) and have been shown to be effective as a physiological adjuvant for eliciting prophylactic or therapeutic antitumor immunity (see Timmerman and Levy, *Ann. Rev. Med.* 50:507-529, 1999). In general, dendritic cells may be identified based on their typical shape (stellate *in situ*, with marked cytoplasmic processes (dendrites) visible *in vitro*), their ability to take up, process and present antigens with high efficiency and their ability to activate naïve T cell responses. Dendritic cells may, of course, be engineered to express specific cell-surface receptors or ligands that are not commonly found on dendritic cells *in vivo* or *ex vivo*, and such modified dendritic cells are contemplated by the present invention. As an alternative to dendritic cells, secreted vesicles antigen-loaded dendritic cells (called exosomes) may be used within a vaccine (see Zitvogel et al., *Nature Med.* 4:594-600, 1998).

Dendritic cells and progenitors may be obtained from peripheral blood, bone marrow, tumor-infiltrating cells, peritumoral tissues-infiltrating cells, lymph nodes, spleen, skin, umbilical cord blood or any other suitable tissue or fluid. For example, dendritic cells may be differentiated *ex vivo* by adding a combination of cytokines such as GM-CSF, IL-4, IL-13 and/or TNF α to cultures of monocytes harvested from peripheral blood. Alternatively, CD34 positive cells harvested from peripheral blood, umbilical cord blood or bone marrow may be differentiated into dendritic cells by adding to the culture medium combinations of GM-CSF, IL-3, TNF α , CD40 ligand, LPS, flt3 ligand and/or other compound(s) that induce differentiation, maturation and proliferation of dendritic cells.

Dendritic cells are conveniently categorized as "immature" and "mature" cells, which allows a simple way to discriminate between two well characterized phenotypes. However, this nomenclature should not be construed to exclude all possible

intermediate stages of differentiation. Immature dendritic cells are characterized as APC with a high capacity for antigen uptake and processing, which correlates with the high expression of Fcγ receptor and mannose receptor. The mature phenotype is typically characterized by a lower expression of these markers, but a high expression of cell surface molecules responsible for T cell activation such as class I and class II MHC, adhesion molecules (e.g., CD54 and CD11) and costimulatory molecules (e.g., CD40, CD80, CD86 and 4-1BB).

APCs may generally be transfected with a polynucleotide encoding a polypeptide of the present invention (or portion or other variant thereof) such that the polypeptide, or an immunogenic portion thereof, is expressed on the cell surface. Such transfection may take place *ex vivo*, and a composition or vaccine comprising such transfected cells may then be used for therapeutic purposes, as described herein. Alternatively, a gene delivery vehicle that targets a dendritic or other antigen presenting cell may be administered to a patient, resulting in transfection that occurs *in vivo*. *In vivo* and *ex vivo* transfection of dendritic cells, for example, may generally be performed using any methods known in the art, such as those described in WO 97/24447, or the gene gun approach described by Mahvi et al., *Immunology and cell Biology* 75:456-460, 1997. Antigen loading of dendritic cells may be achieved by incubating dendritic cells or progenitor cells with the polypeptide, DNA (naked or within a plasmid vector) or RNA; or with antigen-expressing recombinant bacterium or viruses (e.g., vaccinia, fowlpox, adenovirus or lentivirus vectors). Prior to loading, the polypeptide may be covalently conjugated to an immunological partner that provides T cell help (e.g., a carrier molecule). Alternatively, a dendritic cell may be pulsed with a non-conjugated immunological partner, separately or in the presence of the polypeptide.

Vaccines and pharmaceutical compositions may be presented in unit-dose or multi-dose containers, such as sealed ampoules or vials. Such containers are preferably hermetically sealed to preserve sterility of the formulation until use. In general, formulations may be stored as suspensions, solutions or emulsions in oily or aqueous vehicles. Alternatively, a vaccine or pharmaceutical composition may be stored in a freeze-dried condition requiring only the addition of a sterile liquid carrier

immediately prior to use.

The above pharmaceutical compositions and vaccines may be used, for example, for the therapy of breast cancer in a patient. As used herein, a "patient" refers to any warm-blooded animal, preferably a human. A patient may or may not be afflicted with breast cancer. Accordingly, the above pharmaceutical compositions and vaccines may be used to prevent the development of breast cancer or to treat a patient afflicted with breast cancer. In a preferred embodiment, the compounds are administered either prior to or following surgical removal of primary tumors and/or treatment by administration of radiotherapy and conventional chemotherapeutic drugs. To prevent or slow the development of breast cancer, a pharmaceutical composition or vaccine comprising one or more polypeptides as described herein may be administered to a patient. Alternatively, naked DNA or plasmid or viral vector encoding the polypeptide may be administered. For treating a patient with breast cancer, the pharmaceutical composition or vaccine may comprise one or more polypeptides, antibodies or polynucleotides complementary to DNA encoding a polypeptide as described herein (e.g., antisense RNA or antisense deoxyribonucleotide oligonucleotides).

Routes and frequency of administration, as well as dosage, will vary from individual to individual. In general, the pharmaceutical compositions and vaccines may be administered by injection (e.g., intracutaneous, intramuscular, intravenous or subcutaneous), intranasally (e.g., by aspiration) or orally. Between 1 and 10 doses may be administered for a 52-week period. Preferably, 6 doses are administered, at intervals of 1 month, and booster vaccinations may be given periodically thereafter. Alternate protocols may be appropriate for individual patients. A suitable dose is an amount of a compound that, when administered as described above, is capable of promoting an anti-tumor immune response. Such response can be monitored by measuring the anti-tumor antibodies in a patient or by vaccine-dependent generation of cytolytic effector cells capable of killing the patient's tumor cells *in vitro*. Such vaccines should also be capable of causing an immune response that leads to an improved clinical outcome (e.g., more frequent remissions, complete or partial or longer disease-free survival) in vaccinated patients as compared to non-vaccinated patients. In general, for pharmaceutical

compositions and vaccines comprising one or more polypeptides, the amount of each polypeptide present in a dose ranges from about 100 µg to 5 mg. Suitable dose sizes will vary with the size of the patient, but will typically range from about 0.1 mL to about 5 mL.

5 Polypeptides disclosed herein may also be employed in adoptive immunotherapy for the treatment of cancer. Adoptive immunotherapy may be broadly classified into either active or passive immunotherapy. In active immunotherapy, treatment relies on the *in vivo* stimulation of the endogenous host immune system to react against tumors with the administration of immune response-modifying agents (for
10 example, tumor vaccines, bacterial adjuvants, and/or cytokines).

In passive immunotherapy, treatment involves the delivery of biologic reagents with established tumor-immune reactivity (such as effector cells or antibodies) that can directly or indirectly mediate antitumor effects and does not necessarily depend on an intact host immune system. Examples of effector cells include T lymphocytes (for
15 example, CD8+ cytotoxic T-lymphocyte, CD4+ T-helper, tumor-infiltrating lymphocytes), killer cells (Natural Killer cells, lymphokine-activated killer cells), B cells, or antigen presenting cells (such as dendritic cells and macrophages) expressing the disclosed antigens. The polypeptides disclosed herein may also be used to generate antibodies or anti-idiotypic antibodies (as in U.S. Patent No. 4,918,164), for passive
20 immunotherapy.

The predominant method of procuring adequate numbers of T-cells for adoptive immunotherapy is to grow immune T-cells *in vitro*. Culture conditions for expanding single antigen-specific T-cells to several billion in number with retention of antigen recognition *in vivo* are well known in the art. These *in vitro* culture conditions
25 typically utilize intermittent stimulation with antigen, often in the presence of cytokines, such as IL-2, and non-dividing feeder cells. As noted above, the immunoreactive polypeptides described herein may be used to rapidly expand antigen-specific T cell cultures in order to generate sufficient number of cells for immunotherapy. In particular, antigen-presenting cells, such as dendritic, macrophage or B-cells, may be pulsed with
30 immunoreactive polypeptides or transfected with a polynucleotide sequence(s), using

standard techniques well known in the art. For cultured T-cells to be effective in therapy, the cultured T-cells must be able to grow and distribute widely and to survive long term *in vivo*. Studies have demonstrated that cultured T-cells can be induced to grow *in vivo* and to survive long term in substantial numbers by repeated stimulation with antigen supplemented with IL-2 (see, for example, Cheever et al. *Ibid*).

The polypeptides disclosed herein may also be employed to generate and/or isolate tumor-reactive T-cells, which can then be administered to the patient. In one technique, antigen-specific T-cell lines may be generated by *in vivo* immunization with short peptides corresponding to immunogenic portions of the disclosed polypeptides. The resulting antigen specific CD8+ CTL clones may be isolated from the patient, expanded using standard tissue culture techniques, and returned to the patient.

Alternatively, peptides corresponding to immunogenic portions of the polypeptides may be employed to generate tumor reactive T cell subsets by selective *in vitro* stimulation and expansion of autologous T cells to provide antigen-specific T cells which may be subsequently transferred to the patient as described, for example, by Chang et al. (*Crit. Rev. Oncol. Hematol.*, 22(3), 213, 1996).

In another embodiment, syngeneic or autologous dendritic cells may be pulsed with peptides corresponding to at least an immunogenic portion of a polypeptide disclosed herein. The resulting antigen-specific dendritic cells may either be transferred into a patient, or employed to stimulate T cells to provide antigen-specific T cells which may, in turn, be administered to a patient. The use of peptide-pulsed dendritic cells to generate antigen-specific T cells and the subsequent use of such antigen-specific T cells to eradicate tumors in a murine model has been demonstrated by Cheever et al. ("Therapy With Cultured T Cells: Principles Revisited," *Immunological Reviews*, 157:177, 1997).

Additionally vectors expressing the disclosed polynucleotides may be introduced into stem cells taken from the patient and clonally propagated *in vitro* for autologous transplant back into the same patient. In one embodiment, cells of the immune system, such as T cells, may be isolated from the peripheral blood of a patient, using a commercially available cell separation system, such as CellPro Incorporated's (Bothell,

WA) CEPRATE™ system (see U.S. Patent No. 5,240,856; U.S. Patent No. 5,215,926; WO 89/06280; WO 91/16116 and WO 92/07243). The separated cells are stimulated with one or more of the immunoreactive polypeptides contained within a delivery vehicle, such as a microsphere, to provide antigen-specific T cells. The population of tumor antigen-specific T cells is then expanded using standard techniques and the cells are administered back to the patient.

The following Examples are offered by way of illustration and not by way of limitation.

EXAMPLES

EXAMPLE 1

PREPARATION OF BREAST TUMOR-SPECIFIC CDNAS USING

DIFFERENTIAL DISPLAY RT-PCR

This Example illustrates the preparation of cDNA molecules encoding breast tumor-specific polypeptides using a differential display screen.

A. Preparation of B18Ag1 cDNA and Characterization of mRNA Expression

Tissue samples were prepared from breast tumor and normal tissue of a patient with breast cancer that was confirmed by pathology after removal from the patient. Normal RNA and tumor RNA was extracted from the samples and mRNA was isolated and converted into cDNA using a (dT)₁₂AG (SEQ ID NO:130) anchored 3' primer. Differential display PCR was then executed using a randomly chosen primer (CTTCAACCTC) (SEQ ID NO:103). Amplification conditions were standard buffer containing 1.5 mM MgCl₂, 20 pmol of primer, 500 pmol dNTP, and 1 unit of *Taq* DNA polymerase (Perkin-Elmer, Branchburg, NJ). Forty cycles of amplification were performed using 94°C denaturation for 30 seconds, 42°C annealing for 1 minute, and 72°C extension for 30 seconds. An RNA fingerprint containing 76 amplified products was

obtained. Although the RNA fingerprint of breast tumor tissue was over 98% identical to that of the normal breast tissue, a band was repeatedly observed to be specific to the RNA fingerprint pattern of the tumor. This band was cut out of a silver stained gel, subcloned into the T-vector (Novagen, Madison, WI) and sequenced.

5 The sequence of the cDNA, referred to as B18Ag1, is provided in SEQ ID NO:1. A database search of GENBANK and EMBL revealed that the B18Ag1 fragment initially cloned is 77% identical to the endogenous human retroviral element S71, which is a truncated retroviral element homologous to the Simian Sarcoma Virus (SSV). S71 contains an incomplete *gag* gene, a portion of the *pol* gene and an LTR-like structure at 10 the 3' terminus (see Werner et al., *Virology* 174:225-238 (1990)). B18Ag1 is also 64% identical to SSV in the region corresponding to the P30 (*gag*) locus. B18Ag1 contains three separate and incomplete reading frames covering a region which shares considerable homology to a wide variety of *gag* proteins of retroviruses which infect mammals. In addition, the homology to S71 is not just within the *gag* gene, but spans 15 several kb of sequence including an LTR.

B18Ag1-specific PCR primers were synthesized using computer analysis guidelines. RT-PCR amplification (94°C, 30 seconds; 60°C → 42°C, 30 seconds; 72°C, 30 seconds for 40 cycles) confirmed that B18Ag1 represents an actual mRNA sequence present at relatively high levels in the patient's breast tumor tissue. The primers used in 20 amplification were B18Ag1-1 (CTG CCT GAG CCA CAA ATG) (SEQ ID NO:128) and B18Ag1-4 (CCG GAG GAG GAA GCT AGA GGA ATA) (SEQ ID NO:129) at a 3.5 mM magnesium concentration and a pH of 8.5, and B18Ag1-2 (ATG GCT ATT TTC GGG GCC TGA CA) (SEQ ID NO:126) and B18Ag1-3 (CCG GTA TCT CCT CGT GGG TAT T) (SEQ ID NO:127) at 2 mM magnesium at pH 9.5. The same experiments 25 showed exceedingly low to nonexistent levels of expression in this patient's normal breast tissue (see Figure 1). RT-PCR experiments were then used to show that B18Ag1 mRNA is present in nine other breast tumor samples (from Brazilian and American patients) but absent in, or at exceedingly low levels in, the normal breast tissue corresponding to each cancer patient. RT-PCR analysis has also shown that the B18Ag1 30 transcript is not present in various normal tissues (including lymph node, myocardium

and liver) and present at relatively low levels in PBMC and lung tissue. The presence of B18Ag1 mRNA in breast tumor samples, and its absence from normal breast tissue, has been confirmed by Northern blot analysis, as shown in Figure 2.

The differential expression of B18Ag1 in breast tumor tissue was also confirmed by RNase protection assays. Figure 3 shows the level of B18Ag1 mRNA in various tissue types as determined in four different RNase protection assays. Lanes 1-12 represent various normal breast tissue samples, lanes 13-25 represent various breast tumor samples; lanes 26-27 represent normal prostate samples; lanes 28-29 represent prostate tumor samples; lanes 30-32 represent colon tumor samples; lane 33 represents normal aorta; lane 34 represents normal small intestine; lane 35 represents normal skin, lane 36 represents normal lymph node; lane 37 represents normal ovary; lane 38 represents normal liver; lane 39 represents normal skeletal muscle; lane 40 represents a first normal stomach sample; lane 41 represents a second normal stomach sample; lane 42 represents a normal lung; lane 43 represents normal kidney; and lane 44 represents normal pancreas. Interexperimental comparison was facilitated by including a positive control RNA of known β -actin message abundance in each assay and normalizing the results of the different assays with respect to this positive control.

RT-PCR and Southern Blot analysis has shown the B18Ag1 locus to be present in human genomic DNA as a single copy endogenous retroviral element. A genomic clone of approximately 12-18 kb was isolated using the initial B18Ag1 sequence as a probe. Four additional subclones were also isolated by XbaI digestion. Additional retroviral sequences obtained from the ends of the XbaI digests of these clones (located as shown in Figure 4) are shown as SEQ ID NO:3 - SEQ ID NO:10, where SEQ ID NO:3 shows the location of the sequence labeled 10 in Figure 4, SEQ ID NO:4 shows the location of the sequence labeled 11-29, SEQ ID NO:5 shows the location of the sequence labeled 3, SEQ ID NO:6 shows the location of the sequence labeled 6, SEQ ID NO:7 shows the location of the sequence labeled 12, SEQ ID NO:8 shows the location of the sequence labeled 13, SEQ ID NO:9 shows the location of the sequence labeled 14 and SEQ ID NO:10 shows the location of the sequence labeled 11-22.

Subsequent studies demonstrated that the 12-18 kb genomic clone contains a retroviral element of about 7.75 kb, as shown in Figures 5A and 5B. The sequence of this retroviral element is shown in SEQ ID NO: 141. The numbered line at the top of Figure 5A represents the sense strand sequence of the retroviral genomic clone. The box below this line shows the position of selected restriction sites. The arrows depict the different overlapping clones used to sequence the retroviral element. The direction of the arrow shows whether the single-pass subclone sequence corresponded to the sense or anti-sense strand. Figure 5B is a schematic diagram of the retroviral element containing B15Ag1 depicting the organization of viral genes within the element. The open boxes correspond to predicted reading frames, starting with a methionine, found throughout the element. Each of the six likely reading frames is shown, as indicated to the left of the boxes, with frames 1-3 corresponding to those found on the sense strand. Using the cDNA of SEQ ID NO:1 as a probe, a longer cDNA was obtained (SEQ ID NO:227) which contains minor nucleotide differences (less than 1%) compared to the genomic sequence shown in SEQ ID NO:141.

B. Preparation of cDNA Molecules Encoding Other Breast Tumor-Specific Polypeptides

Normal RNA and tumor RNA was prepared and mRNA was isolated and converted into cDNA using a (dT)₁₂AG anchored 3' primer, as described above. Differential display PCR was then executed using the randomly chosen primers of SEQ ID NO: 87-125. Amplification conditions were as noted above, and bands observed to be specific to the RNA fingerprint pattern of the tumor were cut out of a silver stained gel, subcloned into either the T-vector (Novagen, Madison, WI) or the pCRII vector (Invitrogen, San Diego, CA) and sequenced. The sequences are provided in SEQ ID NO:11 - SEQ ID NO:86. Of the 79 sequences isolated, 67 were found to be novel (SEQ ID NO:11-26 and 28-77) (*see also* Figures 6-20).

An extended DNA sequence (SEQ ID NO: 290) for the antigen B15Ag1 (originally identified partial sequence provided in SEQ ID NO: 27) was obtained in further studies. Comparison of the sequence of SEQ ID NO: 290 with those in the gene bank as described above, revealed homology to the known human β -A activin gene.

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Further studies led to the isolation of the full-length cDNA sequence for the antigen B21GT2 (also referred to as B311D; originally identified partial cDNA sequence provided in SEQ ID NO: 56). The full-length sequence is provided in SEQ ID NO: 307, with the corresponding amino acid sequence being provided in SEQ ID NO: 308.

Further studies led to the isolation of a splice variant of B311D. The B311D clone of SEQ ID NO: 316 was sequenced and a XhoI/NotI fragment from this clone was gel purified and 32P-cDTP labeled by random priming for use as a probe for further screening to obtain additional B311D gene sequence. Two fractions of a human breast tumor cDNA bacterial library were screened using standard techniques. One of the clones isolated in this manner yielded additional sequence which includes a poly A+ tail. The determined cDNA sequence of this clone (referred to as B311D_BT1_1A) is provided in SEQ ID NO: 317. The sequences of SEQ ID NO: 316 and 317 were found to share identity over a 464 bp region, with the sequences diverging near the poly A+ sequence of SEQ ID NO: 317.

Subsequent studies identified an additional 146 sequences (SEQ ID NOS:142-289), of which 115 appeared to be novel (SEQ ID NOS:142, 143, 146-152, 154-166, 168-176, 178-192, 194-198, 200-204, 206, 207, 209-214, 216, 218, 219, 221-240, 243-245, 247, 250, 251, 253, 255, 257-266, 268, 269, 271-273, 275, 276, 278, 280, 281, 284, 288 and 291). To the best of the inventors' knowledge none of the previously identified sequences have heretofore been shown to be expressed at a greater level in human breast tumor tissue than in normal breast tissue.

In further studies, several different splice forms of the antigen B11Ag1 (also referred to as B305D) were isolated, with each of the various splice forms containing slightly different versions of the B11Ag1 coding frame. Splice junction sequences define individual exons which, in various patterns and arrangements, make up the various splice forms. Primers were designed to examine the expression pattern of each of the exons using RT-PCR as described below. Each exon was found to show the same expression pattern as the original B11Ag1 clone, with expression being breast tumor-, normal prostate- and normal testis-specific. The determined cDNA sequences for the isolated protein coding exons are provided in SEQ ID NO: 292-298, respectively.

The predicted amino acid sequences corresponding to the sequences of SEQ ID NO: 292 and 298 are provided in SEQ ID NO: 299 and 300. Additional studies using rapid amplification of cDNA ends (RACE), a 5' specific primer to one of the splice forms of B11Ag1 provided above and a breast adenocarcinoma, led to the isolation of three additional, related, splice forms referred to as isoforms B11C-15, B11C-8 and B11C-9,16. The determined cDNA sequences for these isoforms are provided in SEQ ID NO: 301-303, with the corresponding predicted amino acid sequences being provided in SEQ ID NO: 304-306.

In subsequent studies on B305D isoform A (cDNA sequence provided in SEQ ID NO: 292), the cDNA sequence (provided in SEQ ID NO: 313) was found to contain an additional guanine residue at position 884, leading to a frameshift in the open reading frame. The determined DNA sequence of this ORF is provided in SEQ ID NO: 314. This frameshift generates a protein sequence (provided in SEQ ID NO: 315) of 293 amino acids that contains the C-terminal domain common to the other isoforms of B305D but that differs in the N-terminal region.

EXAMPLE 2

PREPARATION OF B18AG1 DNA FROM HUMAN GENOMIC DNA

This Example illustrates the preparation of B18Ag1 DNA by amplification from human genomic DNA.

B18Ag1-DNA may be prepared from 250 ng human genomic DNA using 20 pmol of B18Ag1 specific primers, 500 pmol dNTPS and 1 unit of *Taq* DNA polymerase (Perkin Elmer, Branchburg, NJ) using the following amplification parameters: 94°C for 30 seconds denaturing, 30 seconds 60°C to 42°C touchdown annealing in 2°C increments every two cycles and 72°C extension for 30 seconds. The last increment (a 42°C annealing temperature) should cycle 25 times. Primers were selected using computer analysis. Primers synthesized were B18Ag1-1, B18Ag1-2, B18Ag1-3, and B18Ag1-4. Primer pairs that may be used are 1+3, 1+4, 2+3, and 2+4.

Following gel electrophoresis, the band corresponding to B18Ag1 DNA may be excised and cloned into a suitable vector.

EXAMPLE 3

PREPARATION OF B18Ag1 DNA FROM BREAST TUMOR cDNA

This Example illustrates the preparation of B18Ag1 DNA by amplification from human breast tumor cDNA.

First strand cDNA is synthesized from RNA prepared from human breast tumor tissue in a reaction mixture containing 500 ng poly A+ RNA, 200 pmol of the primer (T)₁₂AG (i.e., TTT TTT TTT TTT AG) (SEQ ID NO: 130), 1X first strand reverse transcriptase buffer, 6.7 mM DTT, 500 mmol dNTPs, and 1 unit AMV or MMLV reverse transcriptase (from any supplier, such as Gibco-BRL (Grand Island, NY)) in a final volume of 30 µl. After first strand synthesis, the cDNA is diluted approximately 25 fold and 1 µl is used for amplification as described in Example 2. While some primer pairs can result in a heterogeneous population of transcripts, the primers B18Ag1-2 (5'ATG GCT ATT TTC GGG GGC TGA CA) (SEQ ID NO: 126) and B18Ag1-3 (5'CCG GTA TCT CCT CGT GGG TAT T) (SEQ ID NO: 127) yield a single 151 bp amplification product.

EXAMPLE 4

IDENTIFICATION OF B-CELL AND T-CELL EPITOPES OF B18Ag1

This Example illustrates the identification of B18Ag1 epitopes.

The B18Ag1 sequence can be screened using a variety of computer algorithms. To determine B-cell epitopes, the sequence can be screened for hydrophobicity and hydrophilicity values using the method of Hopp, *Prog. Clin. Biol. Res.* 172B:367-77 (1985) or, alternatively, Cease et al., *J. Exp. Med.* 164:1779-84 (1986) or Spouge et al., *J. Immunol.* 138:204-12 (1987). Additional Class II MHC (antibody or B-cell) epitopes can be predicted using programs such as AMPHI (e.g., Margalit et al., *J.*

Immunol. 138:2213 (1987)) or the methods of Rothbard and Taylor (e.g., *EMBO J.* 7:93 (1988)).

Once peptides (15-20 amino acids long) are identified using these techniques, individual peptides can be synthesized using automated peptide synthesis equipment (available from manufacturers such as Perkin Elmer/Applied Biosystems Division, Foster City, CA) and techniques such as Merrifield synthesis. Following synthesis, the peptides can be used to screen sera harvested from either normal or breast cancer patients to determine whether patients with breast cancer possess antibodies reactive with the peptides. Presence of such antibodies in breast cancer patient would confirm the immunogenicity of the specific B-cell epitope in question. The peptides can also be tested for their ability to generate a serologic or humoral immune response in animals (mice, rats, rabbits, chimps etc.) following immunization *in vivo*. Generation of a peptide-specific antiserum following such immunization further confirms the immunogenicity of the specific B-cell epitope in question.

To identify T-cell epitopes, the B18Ag1 sequence can be screened using different computer algorithms which are useful in identifying 8-10 amino acid motifs within the B18Ag1 sequence which are capable of binding to HLA Class I MHC molecules. (see, e.g., Rammensee et al., *Immunogenetics* 41:178-228 (1995)). Following synthesis such peptides can be tested for their ability to bind to class I MHC using standard binding assays (e.g., Sette et al., *J. Immunol.* 153:5586-92 (1994)) and more importantly can be tested for their ability to generate antigen reactive cytotoxic T-cells following *in vitro* stimulation of patient or normal peripheral mononuclear cells using, for example, the methods of Bakker et al., *Cancer Res.* 55:5330-34 (1995); Visseren et al., *J. Immunol.* 154:3991-98 (1995); Kawakami et al., *J. Immunol.* 154:3961-68 (1995); and Kast et al., *J. Immunol.* 152:3904-12 (1994). Successful *in vitro* generation of T-cells capable of killing autologous (bearing the same Class I MHC molecules) tumor cells following *in vitro* peptide stimulation further confirms the immunogenicity of the B18Ag1 antigen. Furthermore, such peptides may be used to generate murine peptide and B18Ag1 reactive cytotoxic T-cells following *in vivo* immunization in mice rendered

transgenic for expression of a particular human MHC Class I haplotype (Vitiello et al., *J. Exp. Med.* 173:1007-15 (1991).

A representative list of predicted B18Ag1 B-cell and T-cell epitopes, broken down according to predicted HLA Class I MHC binding antigen, is shown below:

Predicted Th Motifs (B-cell epitopes) (SEQ ID NOS.: 131-133)

SSGGRTFDDFHRVLLVGI

QGAAQKPINLSKXIEVVQGHDE

SPGVFLEHLQEAYRIYTPFDLSA

Predicted HLA A2.1 Motifs (T-cell epitopes) (SEQ ID NOS.: 134-140)

VLLVGIQGA

GAAQKPINL

NLSKXIEVV

EVVQGHDES

HLQEAYRIY

NLAFVAQAA

FVAQAAPDS

EXAMPLE 5

IDENTIFICATION OF T-CELL EPITOPES OF B11Ag1

This Example illustrates the identification of B11Ag1 (also referred to as B305D) epitopes. Four peptides, referred to as B11-8, B11-1, B11-5 and B11-12 (SEQ ID NO: 309-312, respectively) were derived from the B11Ag1 gene.

Human CD8 T cells were primed *in vitro* to the peptide B11-8 using dendritic cells according to the protocol of Van Tsai et al. (*Critical Reviews in Immunology* 18:65-75, 1998). The resulting CD8 T cell cultures were tested for their ability to recognize the B11-8 peptide or a negative control peptide, presented by the B-LCL line, JY. Briefly, T cells were incubated with autologous monocytes in the presence of 10 ug/ml peptide, 10 ng/ml IL-7 and 10 ug/ml IL-2, and assayed for their ability to

specifically lyse target cells in a standard 51-Cr release assay. As shown in Fig. 22, the bulk culture line demonstrated strong recognition of the B11-8 peptide with weaker recognition of the peptide B11-1.

A clone from this CTL line was isolated following rapid expansion using the monoclonal antibody OKT3 and human IL-2. As shown in Fig. 23, this clone (referred to as A1), in addition to being able to recognize specific peptide, recognized JY LCL transduced with the B11Ag1 gene. This data demonstrates that B11-8 is a naturally processed epitope of the B11Ag1 gene. In addition these T cells were further found to recognize and lyse, in an HLA-A2 restricted manner, an established tumor cell line naturally expressing B11Ag1 (Fig. 24). The T cells strongly recognize a lung adenocarcinoma (LT-140-22) naturally expressing B11Ag1 transduced with HLA-A2, as well as an A2+ breast carcinoma (CAMA-1) transduced with B11Ag1, but not untransduced lines or another negative tumor line (SW620).

These data clearly demonstrate that these human T cells recognize not only B11-specific peptides but also transduced cells, as well as, naturally expressing tumor lines.

CTL lines raised against the antigens B11-5 and B11-12, using the procedures described above, were found to recognize corresponding peptide-coated targets.

CHARACTERIZATION OF BREAST TUMOR GENES DISCOVERED BY
DIFFERENTIAL DISPLAY PCR

5 The specificity and sensitivity of the breast tumor genes discovered by differential display PCR were determined using RT-PCR. This procedure enabled the rapid evaluation of breast tumor gene mRNA expression semiquantitatively without using large amounts of RNA. Using gene specific primers, mRNA expression levels in a variety of tissues were examined, including 8 breast tumors, 5 normal breasts, 2 prostate
10 tumors, 2 colon tumors, 1 lung tumor, and 14 other normal adult human tissues, including normal prostate, colon, kidney, liver, lung, ovary, pancreas, skeletal muscle, skin, stomach and testes.

To ensure the semiquantitative nature of the RT-PCR, β -actin was used as internal control for each of the tissues examined. Serial dilutions of the first strand
15 cDNAs were prepared and RT-PCR assays performed using β -actin specific primers. A dilution was then selected that enabled the linear range amplification of β -actin template, and which was sensitive enough to reflect the difference in the initial copy number. Using this condition, the β -actin levels were determined for each reverse transcription reaction from each tissue. DNA contamination was minimized by DNase treatment and
20 by assuring a negative result when using first strand cDNA that was prepared without adding reverse transcriptase.

Using gene specific primers, the mRNA expression levels were determined in a variety of tissues. To date, 38 genes have been successfully examined by RT-PCR, five of which exhibit good specificity and sensitivity for breast tumors
25 (B15AG-1, B31GA1b, B38GA2a, B11A1a and B18AG1a). Figures 21A and 21B depict the results for three of these genes: B15AG-1 (SEQ ID NO:27), B31GA1b (SEQ ID NO:148) and B38GA2a (SEQ ID NO. 157). Table I summarizes the expression level of all the genes tested in normal breast tissue and breast tumors, and also in other tissues.

TABLE I

Percentage of Breast Cancer Antigens that are Expressed in Various Tissues

5	Over-expressed in Breast Tumors	84%
	Breast Tissues	
	Equally Expressed in Normals and Tumor	16%
10	Over-expressed in Breast Tumors but not in any Normal Tissues	9%
	Other Tissues	
	Over-expressed in Breast Tumors but Expressed in Some Normal Tissues	30%
15	Over-expressed in Breast Tumors but Equally Expressed in All Other Tissues	61%

20 From the foregoing, it will be appreciated that, although specific embodiments of the invention have been described herein for the purpose of illustration, various modifications may be made without deviating from the spirit and scope of the invention.

CLAIMS

1. An isolated polypeptide, comprising at least an immunogenic portion of a protein, or a variant thereof, wherein the protein comprises an amino acid sequence that is encoded by a polynucleotide sequence selected from the group consisting of:

(a) sequences recited in SEQ ID NOs: 1, 3-26, 28-77, 142, 143, 146-152, 154-166, 168-176, 178-192, 194-198, 200-204, 206, 207, 209-214, 216, 218, 219, 221-240, 243-245, 247, 250, 251, 253, 255, 257-266, 268, 269, 271-273, 275, 276, 278, 280, 281, 284, 288, 291-298, 301-303, 307, 313, 314, 316 and 317;

(b) sequences that hybridize to a sequence recited in any one of SEQ ID NOs: 1, 3-26, 28-77, 142, 143, 146-152, 154-166, 168-176, 178-192, 194-198, 200-204, 206, 207, 209-214, 216, 218, 219, 221-240, 243-245, 247, 250, 251, 253, 255, 257-266, 268, 269, 271-273, 275, 276, 278, 280, 281, 284, 288, 291-298, 301-303, 307, 313, 314, 316 and 317 under moderately stringent conditions; and

(c) complements of sequences of (a) or (b).

2. An isolated polypeptide according to claim 1, wherein the polypeptide comprises an amino acid sequence that is encoded by a polynucleotide sequence recited in any one of SEQ ID NOs: 1, 3-26, 28-77, 142, 143, 146-152, 154-166, 168-176, 178-192, 194-198, 200-204, 206, 207, 209-214, 216, 218, 219, 221-240, 243-245, 247, 250, 251, 253, 255, 257-266, 268, 269, 271-273, 275, 276, 278, 280, 281, 284, 288, 291-298, 301-303, 307, 313, 314, 316 and 317 or a complement of any of the foregoing polynucleotide sequences.

3. An isolated polypeptide comprising a sequence recited in any one of SEQ ID NOs: 299, 300, 304-306, 308 and 315.

4. An isolated polynucleotide encoding at least 15 amino acid

residues of a protein, or a variant thereof that differs in one or more substitutions, deletions, additions and/or insertions such that the ability of the variant to react with antigen-specific antisera is not substantially diminished, wherein the tumor protein comprises an amino acid sequence that is encoded by a polynucleotide comprising a sequence recited in any one of SEQ ID NOs: 1, 3-26, 28-77, 142, 143, 146-152, 154-166, 168-176, 178-192, 194-198, 200-204, 206, 207, 209-214, 216, 218, 219, 221-240, 243-245, 247, 250, 251, 253, 255, 257-266, 268, 269, 271-273, 275, 276, 278, 280, 281, 284, 288, 291-298, 301-303, 307, 313, 314, 316 and 317 or a complement of any of the foregoing sequences.

10 5. An isolated polynucleotide encoding a protein, or a variant thereof, wherein the tumor protein comprises an amino acid sequence that is encoded by a polynucleotide comprising a sequence recited in any one of SEQ ID NOs: 1, 3-26, 28-77, 142, 143, 146-152, 154-166, 168-176, 178-192, 194-198, 200-204, 206, 207, 209-214, 216, 218, 219, 221-240, 243-245, 247, 250, 251, 253, 255, 257-266, 268, 269, 271-273, 275, 276, 278, 280, 281, 284, 288, 291-298, 301-303, 307, 313, 314, 316 and 317 or a complement of any of the foregoing sequences.

6. An isolated polynucleotide, comprising a sequence recited in any one of SEQ ID Nos: 1, 3-26, 28-77, 142, 143, 146-152, 154-166, 168-176, 178-192, 194-198, 200-204, 206, 207, 209-214, 216, 218, 219, 221-240, 243-245, 247, 250, 251, 253, 255, 257-266, 268, 269, 271-273, 275, 276, 278, 280, 281, 284, 288, 291-298, 301-303, 307, 313, 314, 316 and 317.

25 7. An isolated polynucleotide, comprising a sequence that hybridizes to a sequence recited in any one of SEQ ID NOs: 1, 3-26, 28-77, 142, 143, 146-152, 154-166, 168-176, 178-192, 194-198, 200-204, 206, 207, 209-214, 216, 218, 219, 221-240, 243-245, 247, 250, 251, 253, 255, 257-266, 268, 269, 271-273, 275, 276, 278, 280, 281, 284, 288, 291-298, 301-303, 307, 313, 314, 316 and 317 under moderately stringent conditions.

30

8. An isolated polynucleotide complementary to a polynucleotide according to any one of claims 4-7.

9. An expression vector, comprising a polynucleotide according to any one of claims claim 4-8.

10. A host cell transformed or transfected with an expression vector according to claim 9.

11. An isolated antibody, or antigen-binding fragment thereof, that specifically binds to a protein that comprises an amino acid sequence that is encoded by a polynucleotide sequence recited in any one of SEQ ID NOs: 1, 3-26, 28-77, 142, 143, 146-152, 154-166, 168-176, 178-192, 194-198, 200-204, 206, 207, 209-214, 216, 218, 219, 221-240, 243-245, 247, 250, 251, 253, 255, 257-266, 268, 269, 271-273, 275, 276, 278, 280, 281, 284, 288, 291-298, 301-303, 307, 313, 314, 316 and 317 or a complement of any of the foregoing polynucleotide sequences.

12. A fusion protein, comprising at least one polypeptide according to claim 1.

13. A fusion protein according to claim 12, wherein the fusion protein comprises an expression enhancer that increases expression of the fusion protein in a host cell transfected with a polynucleotide encoding the fusion protein.

14. A fusion protein according to claim 12, wherein the fusion protein comprises a T helper epitope that is not present within the polypeptide of claim 1.

15. A fusion protein according to claim 12, wherein the fusion protein comprises an affinity tag.

16. An isolated polynucleotide encoding a fusion protein according to claim 12.

17. A pharmaceutical composition, comprising a physiologically acceptable carrier and at least one component selected from the group consisting of:

- (a) a polypeptide according to claim 1;
- (b) a polynucleotide according to claim 4;
- (c) an antibody according to claim 11;
- (d) a fusion protein according to claim 12; and
- (e) a polynucleotide according to claim 16.

18. A vaccine comprising an immunostimulant and at least one component selected from the group consisting of:

- (a) a polypeptide according to claim 1;
- (b) a polynucleotide according to claim 4;
- (c) an antibody according to claim 11;
- (d) a fusion protein according to claim 12; and
- (e) a polynucleotide according to claim 16.

19. A vaccine according to claim 18, wherein the immunostimulant is an adjuvant.

20. A vaccine according to any claim 18, wherein the immunostimulant induces a predominantly Type I response.

21. A method for inhibiting the development of a cancer in a patient, comprising administering to a patient an effective amount of a pharmaceutical composition according to claim 17.

22. A method for inhibiting the development of a cancer in a patient, comprising administering to a patient an effective amount of a vaccine according to

claim 18.

23. A pharmaceutical composition comprising an antigen-presenting cell that expresses a polypeptide according to claim 1, in combination with a
5 pharmaceutically acceptable carrier or excipient.

24. A pharmaceutical composition according to claim 23, wherein the antigen presenting cell is a dendritic cell or a macrophage.

10 25. A vaccine comprising an antigen-presenting cell that expresses a polypeptide comprising at least an immunogenic portion of a protein, or a variant thereof, wherein the protein comprises an amino acid sequence that is encoded by a polynucleotide sequence selected from the group consisting of:

(a) sequences recited in SEQ ID NOs: 1, 3-26, 28-86, 142-253, 255-
15 298, 301-303, 307, 313, 314, 316 and 317;

(b) sequences that hybridize to a sequence recited in any one of SEQ ID NOs: 1, 3-26, 28-86, 142-253, 255-298, 301-303, 307, 313, 314, 316 and 317 under moderately stringent conditions; and

(c) complements of sequences of (i) or (ii);
20 in combination with an immunostimulant.

26. A vaccine according to claim 25, wherein the immunostimulant is an adjuvant.

25 27. A vaccine according to claim 25, wherein the immunostimulant induces a predominantly Type I response.

28. A vaccine according to claim 25, wherein the antigen-presenting cell is a dendritic cell.

30 29. A method for inhibiting the development of a cancer in a patient,

comprising administering to a patient an effective amount of an antigen-presenting cell that expresses a polypeptide comprising at least an immunogenic portion of a protein, or a variant thereof, wherein the protein comprises an amino acid sequence that is encoded by a polynucleotide sequence selected from the group consisting of:

5 (a) sequences recited in SEQ ID NOs: 1, 3-26, 28-86, 142-253, 255-298, 301-303, 307, 313, 314, 316 and 317;

(b) sequences that hybridize to a sequence recited in any one of SEQ ID NOs: 1, 3-26, 28-86, 142-253, 255-298, 301-303, 307, 313, 314, 316 and 317 under moderately stringent conditions; and

10 (c) complements of sequences encoded by a polynucleotide recited in any one of SEQ ID NOs: 1, 3-26, 28-86, 142-253, 255-298, 301-303, 307, 313, 314, 316 and 317;

and thereby inhibiting the development of a cancer in the patient.

15 30. A method according to claim 29, wherein the antigen-presenting cell is a dendritic cell.

31. A method according to any one of claims 21, 22 and 29, wherein the cancer is breast cancer.

20 32. A method for removing tumor cells from a biological sample, comprising contacting a biological sample with T cells that specifically react with a protein, wherein the protein comprises an amino acid sequence that is encoded by a polynucleotide sequence selected from the group consisting of:

25 (i) polynucleotides recited in any one of SEQ ID NOs: 1, 3-26, 28-86, 142-253, 255-298, 301-303, 307, 313, 314, 316 and 317; and

(ii) complements of the foregoing polynucleotides;

wherein the step of contacting is performed under conditions and for a time sufficient to permit the removal of cells expressing the antigen from the sample.

30 33. A method according to claim 32, wherein the biological sample is

blood or a fraction thereof.

34. A method for inhibiting the development of a cancer in a patient, comprising administering to a patient a biological sample treated according to the method of claim 32.

35. A method for stimulating and/or expanding T cells specific for a protein, comprising contacting T cells with at least one component selected from the group consisting of:

10 (a) polypeptides comprising at least an immunogenic portion of a protein, or a variant thereof, wherein the protein comprises an amino acid sequence that is encoded by a polynucleotide sequence selected from the group consisting of:

(i) sequences recited in SEQ ID NOs: 1, 3-26, 28-86, 142-253, 255-298, 301-303, 307, 313, 314, 316 and 317;

15 (ii) sequences that hybridize to a sequence recited in any one of SEQ ID NOs: 1, 3-26, 28-86, 142-253, 255-298, 301-303, 307, 313, 314, 316 and 317 under moderately stringent conditions; and

(iii) complements of sequences of (i) or (ii);

(b) polynucleotides encoding a polypeptide of (a); and

20 (c) antigen presenting cells that express a polypeptide of (a);

under conditions and for a time sufficient to permit the stimulation and/or expansion of T cells.

36. An isolated T cell population, comprising T cells prepared according to the method of claim 35.

37. A method for inhibiting the development of a cancer in a patient, comprising administering to a patient an effective amount of a T cell population according to claim 36.

38. A method for inhibiting the development of a cancer in a patient,

comprising the steps of:

(a) incubating CD4⁺ and/or CD8⁺ T cells isolated from a patient with at least one component selected from the group consisting of:

(i) polypeptides comprising at least an immunogenic portion of a protein, or a variant thereof, wherein the protein comprises an amino acid sequence that is encoded by a polynucleotide sequence selected from the group consisting of:

(1) sequences recited in SEQ ID NOs: 1, 3-26, 28-86, 142-253, 255-298, 301-303, 307, 313, 314, 316 and 317;

(2) sequences that hybridize to a sequence recited in any one of SEQ ID NOs: 1, 3-26, 28-86, 142-253, 255-298, 301-303, 307, 313, 314, 316 and 317 under moderately stringent conditions; and

(3) complements of sequences of (1) or (2);

(ii) polynucleotides encoding a polypeptide of (i); and
 (iii) antigen presenting cells that expresses a polypeptide of (i); such that T cells proliferate; and

(b) administering to the patient an effective amount of the proliferated T cells, and thereby inhibiting the development of a cancer in the patient.

20

39. A method for inhibiting the development of a cancer in a patient, comprising the steps of:

(a) incubating CD4⁺ and/or CD8⁺ T cells isolated from a patient with at least one component selected from the group consisting of:

25 (i) polypeptides comprising at least an immunogenic portion of a protein, or a variant thereof, wherein the protein comprises an amino acid sequence that is encoded by a polynucleotide sequence selected from the group consisting of:

(1) sequences recited in SEQ ID NOs: 1, 3-26, 28-86, 142-253, 255-298, 301-303, 307, 313, 314, 316 and 317;

30 (2) sequences that hybridize to a sequence recited in

any one of SEQ ID NOs: 1, 3-26, 28-86, 142-253, 255-298, 301-303, 307, 313, 314, 316 and 317 under moderately stringent conditions; and

- (3) complements of sequences of (1) or (2);
- (ii) polynucleotides encoding a polypeptide of (i); and
- (iii) antigen presenting cells that express a polypeptide of (i);

such that T cells proliferate;

(b) cloning at least one proliferated cell to provide cloned T cells; and

(c) administering to the patient an effective amount of the cloned T cells, and thereby inhibiting the development of a cancer in the patient.

40. A method for determining the presence or absence of a cancer in a patient, comprising the steps of:

(a) contacting a biological sample obtained from a patient with a binding agent that binds to a protein, wherein the protein comprises an amino acid sequence that is encoded by a polynucleotide sequence recited in any one of SEQ ID NOs: 1, 3-26, 28-86, 142-253, 255-298, 301-303, 307, 313, 314, 316 and 317 or a complement of any of the foregoing polynucleotide sequences;

(b) detecting in the sample an amount of polypeptide that binds to the binding agent; and

(c) comparing the amount of polypeptide to a predetermined cut-off value, and therefrom determining the presence or absence of a cancer in the patient.

41. A method according to claim 40, wherein the binding agent is an antibody.

42. A method according to claim 43, wherein the antibody is a monoclonal antibody.

43. A method according to claim 40, wherein the cancer is breast

cancer.

44. A method for monitoring the progression of a cancer in a patient, comprising the steps of:

(a) contacting a biological sample obtained from a patient at a first point in time with a binding agent that binds to a protein, wherein the protein comprises an amino acid sequence that is encoded by a polynucleotide sequence recited in any one of SEQ ID NOs: 1, 3-26, 28-86, 142-253, 255-298, 301-303, 307, 313, 314, 316 and 317 or a complement of any of the foregoing polynucleotide sequences;

(b) detecting in the sample an amount of polypeptide that binds to the binding agent;

(c) repeating steps (a) and (b) using a biological sample obtained from the patient at a subsequent point in time; and

(d) comparing the amount of polypeptide detected in step (c) to the amount detected in step (b) and therefrom monitoring the progression of the cancer in the patient.

45. A method according to claim 44, wherein the binding agent is an antibody.

46. A method according to claim 45, wherein the antibody is a monoclonal antibody.

47. A method according to claim 44, wherein the cancer is a breast cancer.

48. A method for determining the presence or absence of a cancer in a patient, comprising the steps of:

(a) contacting a biological sample obtained from a patient with an oligonucleotide that hybridizes to a polynucleotide that encodes a protein, wherein the protein comprises an amino acid sequence that is encoded by a polynucleotide sequence

recited in any one of SEQ ID NO: 1, 3-26, 28-86, 142-253, 255-298, 301-303, 307, 313, 314, 316 and 317 or a complement of any of the foregoing polynucleotide sequences;

(b) detecting in the sample an amount of a polynucleotide that hybridizes to the oligonucleotide; and

(c) comparing the amount of polynucleotide that hybridizes to the oligonucleotide to a predetermined cut-off value, and therefrom determining the presence or absence of a cancer in the patient.

49. A method according to claim 48, wherein the amount of polynucleotide that hybridizes to the oligonucleotide is determined using a polymerase chain reaction.

50. A method according to claim 48, wherein the amount of polynucleotide that hybridizes to the oligonucleotide is determined using a hybridization assay.

51. A method for monitoring the progression of a cancer in a patient, comprising the steps of:

(a) contacting a biological sample obtained from a patient with an oligonucleotide that hybridizes to a polynucleotide that encodes a protein, wherein the protein comprises an amino acid sequence that is encoded by a polynucleotide sequence recited in any one of SEQ ID NO: 1, 3-26, 28-86, 142-253, 255-298, 301-303, 307, 313, 314, 316 and 317 or a complement of any of the foregoing polynucleotide sequences;

(b) detecting in the sample an amount of a polynucleotide that hybridizes to the oligonucleotide;

(c) repeating steps (a) and (b) using a biological sample obtained from the patient at a subsequent point in time; and

(d) comparing the amount of polynucleotide detected in step (c) to the amount detected in step (b) and therefrom monitoring the progression of the cancer in the patient.

52. A method according to claim 51, wherein the amount of polynucleotide that hybridizes to the oligonucleotide is determined using a polymerase chain reaction.

53. A method according to claim 51, wherein the amount of polynucleotide that hybridizes to the oligonucleotide is determined using a hybridization assay.

54. A diagnostic kit, comprising:

- (a) one or more antibodies according to claim 11; and
- (b) a detection reagent comprising a reporter group.

55. A kit according to claim 54, wherein the antibodies are immobilized on a solid support.

56. A kit according to claim 54, wherein the detection reagent comprises an anti-immunoglobulin, protein G, protein A or lectin.

57. A kit according to claim 54, wherein the reporter group is selected from the group consisting of radioisotopes, fluorescent groups, luminescent groups, enzymes, biotin and dye particles.

58. An oligonucleotide comprising 10 to 40 contiguous nucleotides that hybridize under moderately stringent conditions to a polynucleotide that encodes a protein, wherein the protein comprises an amino acid sequence that is encoded by a polynucleotide sequence recited in any one of SEQ ID NOs: 1, 3-26, 28-77, 142, 143, 146-152, 154-166, 168-176, 178-192, 194-198, 200-204, 206, 207, 209-214, 216, 218, 219, 221-240, 243-245, 247, 250, 251, 253, 255, 257-266, 268, 269, 271-273, 275, 276, 278, 280, 281, 284, 288, 291-298, 301-303, 307, 313, 314, 316 and 317 or a complement of any of the foregoing polynucleotides.

59. A oligonucleotide according to claim 58, wherein the oligonucleotide comprises 10-40 contiguous nucleotides recited in any one of SEQ ID Nos: 1, 3-26, 28-77, 142, 143, 146-152, 154-166, 168-176, 178-192, 194-198, 200-204, 206, 207, 209-214, 216, 218, 219, 221-240, 243-245, 247, 250, 251, 253, 255, 257-266, 268, 269, 271-273, 275, 276, 278, 280, 281, 284, 288, 291-298, 301-303, 307, 313, 314, 316 and 317.

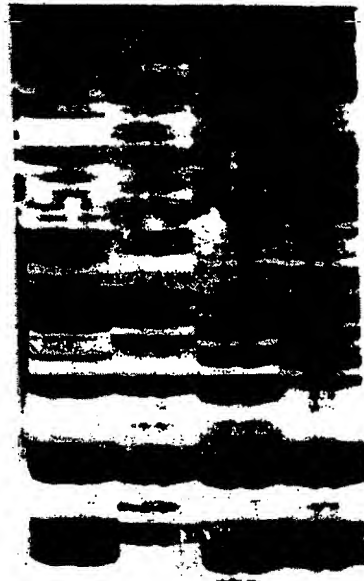
60. A diagnostic kit, comprising:

- (a) an oligonucleotide according to claim 59; and
- (b) a diagnostic reagent for use in a polymerase chain reaction or hybridization assay.

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cDNA PREPARED FROM
NORMAL BREAST TISSUE
FROM THE SAME PATIENT

cDNA PREPARED
FROM BREAST TUMOR



B18Ag1

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BREAST TUMOR mRNA
NORMAL BREAST TISSUE mRNA



Fig. 2

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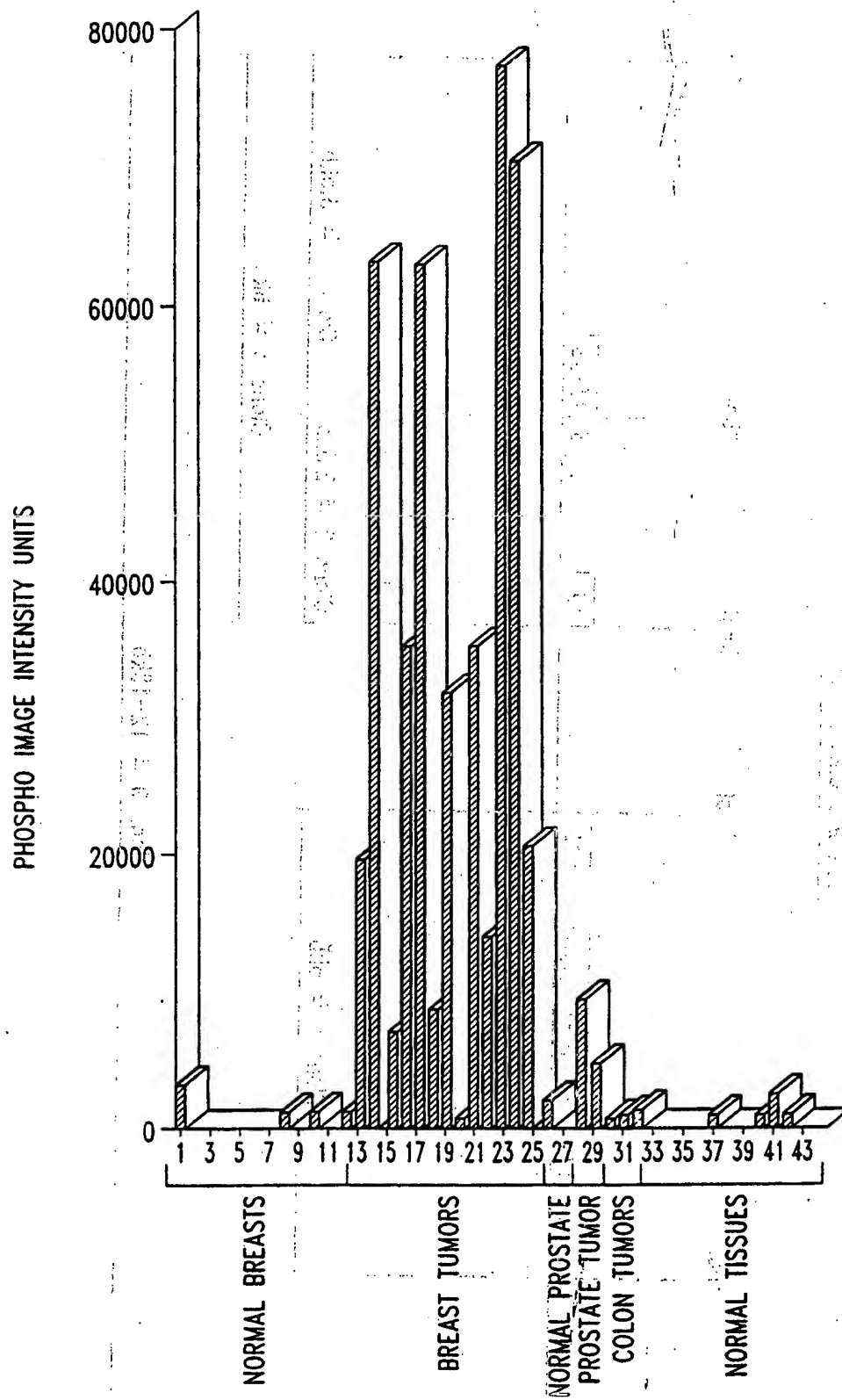


Fig. 3

GENOMIC CLONE MAP

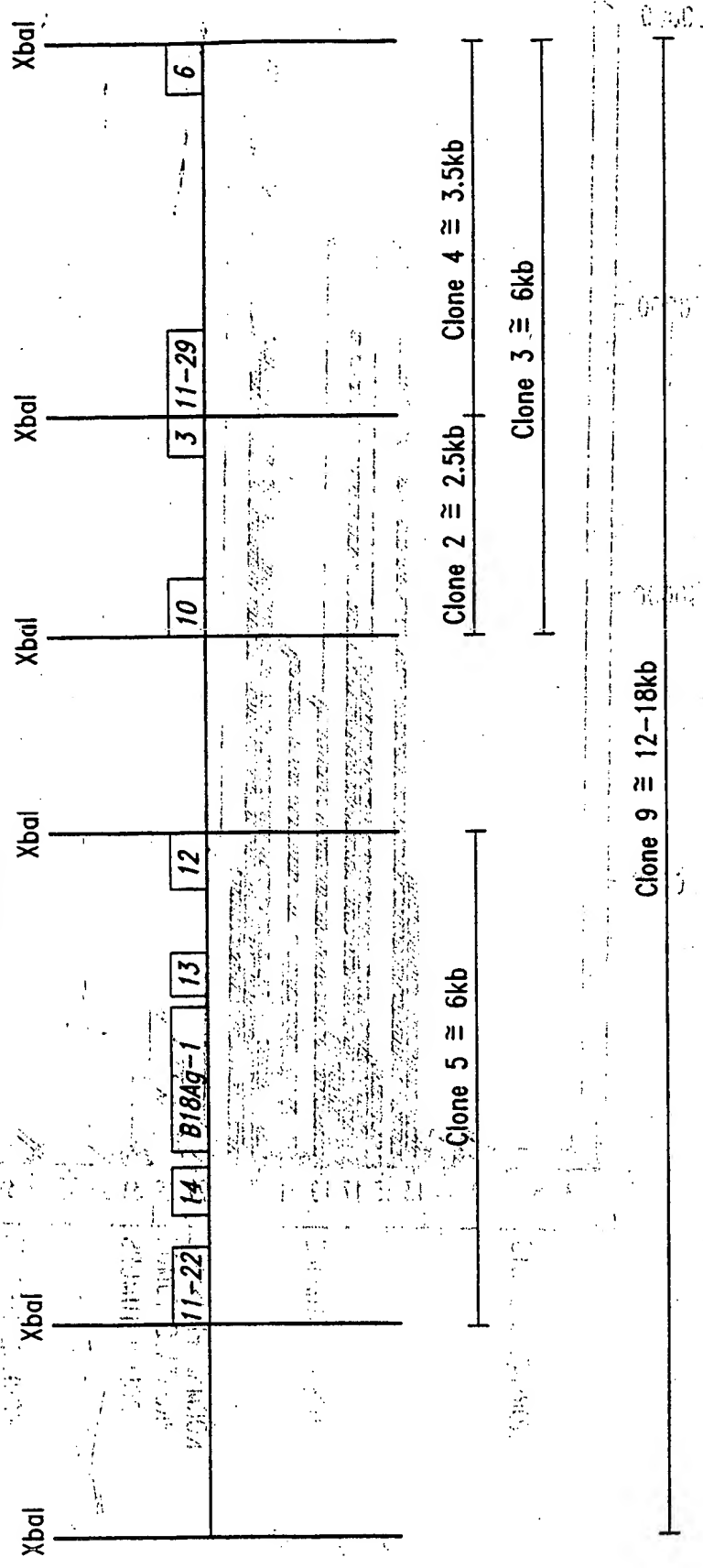


Fig. 4

Fig. 5A

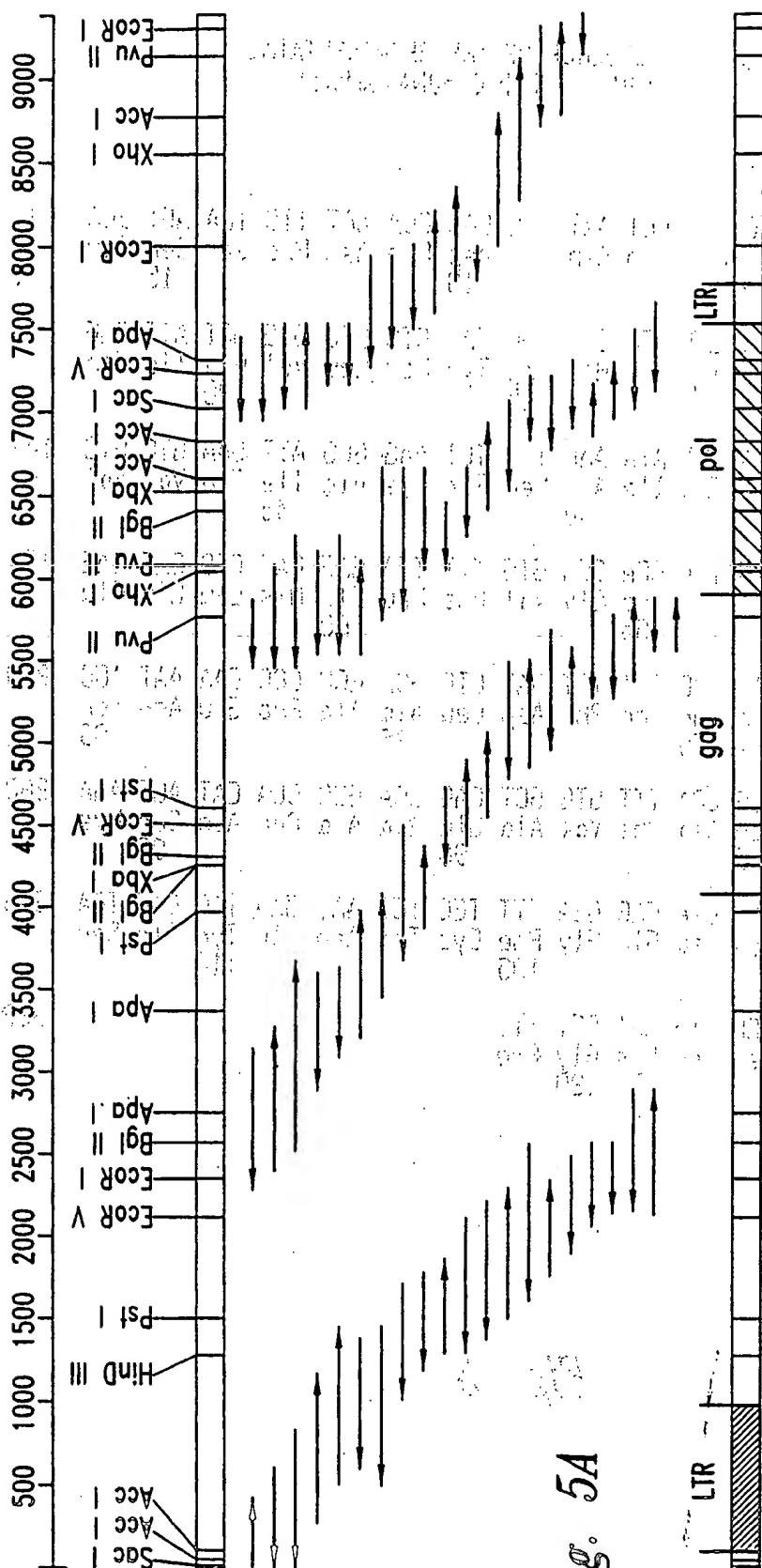
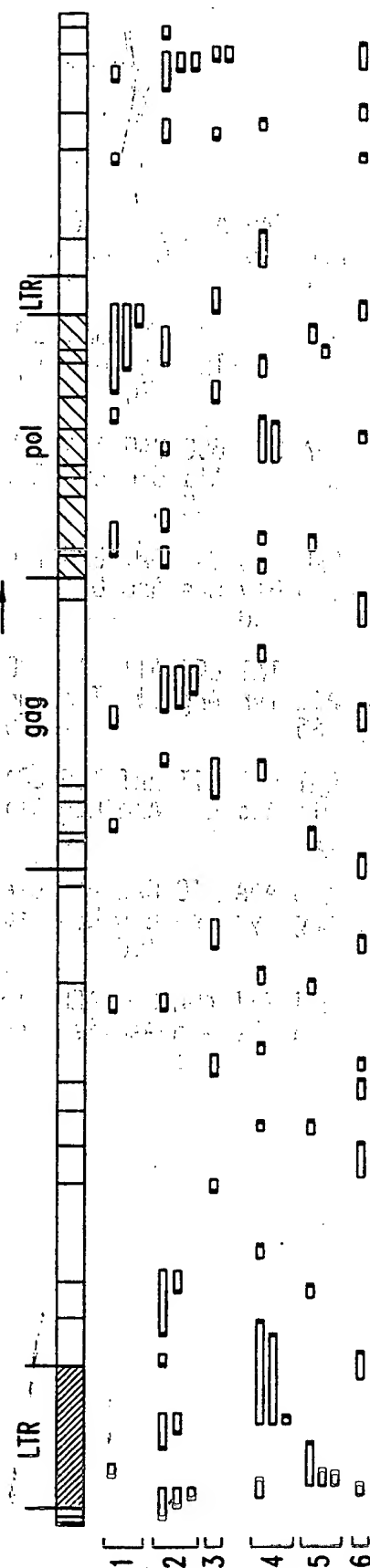


Fig. 5B



NUCLEOTIDE SEQUENCE OF THE REPRESENTATIVE
BREAST-TUMOR SPECIFIC cDNA B18Ag1

TTA	GAG	ACC	CAA	TTG	GGA	CCT	AAT	TGG	GAC	CCA	AAT	TTC	TCA	AGT	GGA	48
Leu	Glu	Thr	Gln	Leu	Gly	Pro	Asn	Trp	Asp	Pro	Asn	Phe	Ser	Ser	Gly	
1				5					10					15		
GGG	AGA	ACT	TTT	GAC	GAT	TTG	CAC	CGG	TAT	CTC	CTC	GTG	GGT	ATT	CAG	96
Gly	Arg	Thr	Phe	Asp	Asp	Phe	His	Arg	Tyr	Leu	Leu	Val	Gly	Ile	Gln	
			20					25					30			
GGA	GCT	GCC	CAG	AAA	CCT	ATA	AAC	TTG	TCT	AAG	GCG	ATT	GAA	GTC	GTC	144
Gly	Ala	Ala	Gln	Lys	Pro	Ile	Asn	Leu	Ser	Lys	Ala	Ile	Glu	Val	Val	
			35				40					45				
CAG	GGG	CAT	GAT	GAG	TCA	CCA	GGA	GTG	TTT	TTA	GAG	CAC	CTC	CAG	GAG	192
Gln	Gly	His	Asp	Glu	Ser	Pro	Gly	Val	Phe	Leu	Glu	His	Leu	Gln	Glu	
	50					55					60					
GCT	TAT	CGG	ATT	TAC	ACC	CCT	TTT	GAC	CTG	GCA	GCC	CCC	GAA	AAT	AGC	240
Ala	Tyr	Arg	Ile	Tyr	Thr	Pro	Phe	Asp	Leu	Ala	Ala	Pro	Glu	Asn	Ser	
65					70				75					80		
CAT	GCT	CTT	AAT	TTG	GCA	TTT	GTG	GCT	CAG	GCA	GCC	CCA	GAT	AGT	AAA	288
His	Ala	Leu	Asn	Leu	Ala	Phe	Val	Ala	Gln	Ala	Ala	Pro	Asp	Ser	Lys	
			85					90						95		
AGG	AAA	CTC	CAA	AAA	CTA	GAG	GGA	TTT	TGC	TGG	AAT	GAA	TAC	CAG	TCA	336
Arg	Lys	Leu	Gln	Lys	Leu	Glu	Gly	Phe	Cys	Trp	Asn	Glu	Tyr	Gln	Ser	
			100				105						110			
GCT	TTT	AGA	GAT	AGC	CTA	AAA	GGT	TTT								363
Ala	Phe	Arg	Asp	Ser	Leu	Lys	Gly	Phe								
		115					120									

Fig. 6

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NUCLEOTIDE SEQUENCE OF THE REPRESENTATIVE
BREAST-TUMOR SPECIFIC cDNA B17Ag1

GC TGGGCACAGT GGCTCATACC TGTAATCCTG ACCGTTTCAG AGGCTCAGGT 60

CG CTTGAGCCCA AGATTCAAG ACTAGTCTGG GTAACATAGT GAGACCCTAT 120

AA AAATAAAAAA ATGAGCCTGG TGTAGTGGCA CACACCAAGCT GAGGAGGGAG 180

CT AGGAGA 196

Fig. 7

NUCLEOTIDE SEQUENCE OF THE REPRESENTATIVE
BREAST-TUMOR SPECIFIC cDNA B17Ag2

GC TTGGGGGCTC TGACTAGAAA TTCAAGGAAC CTGGGATTCA AGTCCAACTG 60
AC TTACTGTG GNTCCAATA AACTGCTTCT TTCCTATTCC CTCTCTATTA 120
AA GGAAAACGAT GTCTGTGTAT AGCCAAGTCA GNTATCCTAA AAGGAGATAC 180
AT TAAATATCAG AATGTAAAAC CTGGGAACCA GGTTCACAGC CTGGGATTAA 240
CA AGAAGACTGA ACAGTACTAC TGTGAAAAGC CCGAAGNGGC AATATGTTCA 300
TT GAAGGATGGC TGGGAGAATG AATGCTCTGT CCCCAGTCC CAAGCTCACT 360
CT CCTTTATAGC CTAGGAGA 388

Fig. 8

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NUCLEOTIDE SEQUENCE OF THE REPRESENTATIVE
BREAST-TUMOR SPECIFIC cDNA B13Ag2a

GC CTATAATCAT GTTTCATT ATTTTCACAT TTTATTAACC AATTTCTGTT 60
AA AATATGAGGG AAATATATGA AACAGGGAGG CAATGTTTCCAG ATAATTGATC 120
TG ATTTCTACAT CAGATGCTCT TTCCTTTCTT GTTTATTTC TTTTATTTC 180
GG TCGAATGTAA TAGCTTTGTT TCAAGAGAGA GTTTTGGCAG TTTCTGTAGC 240
CT GCTCATGTCT CCAGGCATCT ATTTGCACTT TAGGAGGTGT CGTGGGAGAC 300
CT ATTTTTTCCA TATTGGGCA ACTACTA 337

Fig. 9

NUCLEOTIDE SEQUENCE OF THE REPRESENTATIVE
BREAST-TUMOR SPECIFIC cDNA B13Ag1b

GC CATACAGTGC CTTTCCATTT ATTTAACCCC CACCTGAACG GCATAAACTG 60
GC TGGTGTTTTT TACTGTAAAC AATAAGGAGA CTTTGCTCTT CATTTAAACC 120
AT TTCATATTTT ACGCTCGAGG GTTTTACC GTTCCTTTTT ACACTCCTTA 180
TT TAAGTCGTTT GGAACAAGAT ATTTTTCTT TCCTGGCAGC TTTTAACATT 240
TT TGTGCTGGG GGACTGCTGG TCACTGTTT TCACAGTTGC AAATCAAGGC 300
CC AAGAAAAAAA AATTTTTTTG TTTTATTGA AACTGGACCG GATAACGGT 360
CG GCTGCTGTAT ATAGTTTAA ATGGTTTATT GCACCTCCTT AAGTTGCACT 420
GG GGGGNTTTTG NATAGAAAGT NTTTANTCAC ANAGTCACAG GGACTTTTNT 480
NA CTGAGCTAAA AAGGGCTGNT TTTCGGGTGG GGGCAGATGA AGGCTCACAG 540
TC TCTTAGAGGG GGGAACTNCT A 571

Fig. 10

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NUCLEOTIDE SEQUENCE OF THE REPRESENTATIVE
BREAST-TUMOR SPECIFIC cDNA B13Ag1a

TA ATAAC TTAAA TATATTTTGA TCACCCACTG GGGTGATAAG ACAATAGATA 60
TT TCCAAAAAGC ATAAACCAA AGTATCATAC CAAACCAAAT TCATACTGCT 120
CC GCACTGAAAC TTCACCTTCT AACTGTCTAC CTAACCAAAT TCTACCCCTC 180
GG TGGGTGCTCA CTACTCTTTT TTTTTTTTTT TTTNTTTTGG AGATGGAGTC 240
CA GCCCAGGGGT GGAGTACAAT GGCACAACCT CAGCTCACTG NAACCTCCGC 300
TT CATGAGATTC TCCTGNTTCA GCCTTCCCAG TAGCTGGGAC TACAGGTGTG 360
TG CCTGGNTAAT CTTTTTNGT TTTNGGGTAG AGATGGGGGT TTTACATGTT 420
TG GTNTCGAACT CCTGACCTCA AGTGATCCAC CCACTCAGG CTCCCAAAGT 480
TA CAGACATGAG CCACTGNGCC CAGNCCTGGT GCATGCTCAC TTCTCTAGGC 540
548

Fig. 11

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NUCLEOTIDE SEQUENCE OF THE REPRESENTATIVE
BREAST-TUMOR-SPECIFIC cDNA B11Ag1

TG CACATGCAGA ATATTCTATC GGTACTTCAG CTATTACTCA TTTTGATGGC 60
AG CCTATCCTCA AGATGAGTAT TTAGAAAGAA TTGATTTAGC GATAGACCAA 120
GC ACTCTGACTA CACGAAATTG TTCAGATGTG ATGGATTJAT GACAGTTGAT 180
GA GATTATTAAG TGATTATTTT AAAGGGAATC CATTAAATCC AGAATATCTT 240
TC AAGATGATAT AGAAATAGAA CAGAAAGAGA CTACAAATGA AGATGTATCA 300
TA TTGAAGAGCC TATAGTAGAA AATGAATTAG CTGCATTTAT TAGCCTTACA 360
TT TTCCTGATGA ATCTTATATT CAGCCATCGA CATAGCATTG CCTGATGGGC 420
GA ATAATAGAAA CTGGGTGCGG GGCTATTGAT GAATTCATCC NCAGTAAATT 480
AC AAAATATAAC TCGATTGCAT TTGGATGATG GAATACTAAA TCTGGCAAAA 540
GG AGCTACTAGT AACCTCTCTT TTTGAGATGC AAAATTTTCT TTTAGGGTTT 600
CT ACTTTACGGA TATTGGAGCA TAACGGGA 638

Fig. 12

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NUCLEOTIDE SEQUENCE OF THE REPRESENTATIVE
BREAST-TUMOR SPECIFIC cDNA B3CA3c

ACTGATGGAT GTCGCCGGAG GCGAGGGGCC TTATCTGATG CTCGGCTGCC TGTTCTGAT 60
GTGCGCGGCG ATTGGGCTGT TTATCTCAA CACCGCCACG GCGGTGCTGA TGGCGCCTAT 120
TGCCTTAGCG GCGGCGAAGT CAATGGGCGT CTCACCCTAT CCTTTGCCA TGGTGGTGGC 180
GATGGCGGCT TCGGCGGCGT TTATGACCCG GGTCTCCTCG CCGGTTAACA CCCTGGTGCT 240
TGGCCCTGGC AAGTACTCAT TTAGCGATTT TGTCAAATA GGCCTG 286

Fig. 13

NUCLEOTIDE SEQUENCE OF THE REPRESENTATIVE
BREAST-TUMOR SPECIFIC cDNA B9CG1

AG CAGCCCCTTC TTCTCAATTT CATCTGTCAC TACCCTGGTG TAGTATCTCA 60
CA TTTTATAGC CTCCTCCCTG GTCTGTCTTT TGATTTTCCT GCCTGTAATC 120
AC ATAAGTCAA GTAAACATTT CTAAAGTGTG GTATGCTCA TGTCACCTCT 180
AA ATAGTTTCCA TTACCGTCTT AATAAAATTC GGATTGTTC TTCTCTATT 240
CA CCTATGACCG AA 262

Fig. 14

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NUCLEOTIDE SEQUENCE OF THE REPRESENTATIVE
BREAST-TUMOR SPECIFIC cDNA B9CG3

AG CAAAGCCAGT GGTGGAGCT CTCTACTGTG TAAACTCCTA AACCAAGGCC 60
TA AATGGTGGCA GGATTTTAT TATAACATG TACCATGCA AATTCCTAT 120
GA TATATTCTTC TACATTAAA CAATAAAAT AATCTATTT TAAAAGCCTA 180
AG TTAGGTAAGA GTGTTTAATG AGAGGGTATA AGGTATAAT CACCAAGTCAA 240
TG CCTATGACCG A 261

Fig. 15

NUCLEOTIDE SEQUENCE OF THE REPRESENTATIVE
BREAST-TUMOR SPECIFIC cDNA-B2CA2

GG GCATGGACGC AGACGCCTGA CGTTTGGCTG AAAATCTTTC ATTGATTCTG 60
AT AGGAAAATTC CCAAAGAGGG AATGTCCTGT TGCTCGCCAG TTTTNTGTT 120
GG ANAAGGCAAN GAGCTCTTCA GACTATTGNN ATINTCGTTC GGTCTTCTGC 180
CG NCTTGCNANG ATCTTCAT 208

Fig. 16

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NUCLEOTIDE SEQUENCE OF THE REPRESENTATIVE
BREAST-TUMOR SPECIFIC cDNA B3CA1

GG GCATGGACGC AGACGCCTGA CGTTTGCTG AAAATCTTTC ATTGATTCTG 60
AT AGGAAAATTC CCAAAGAGGG AATGTCCTGT TGCTCGCCAG TTTTNTGT 120
GG ANAAGGCAAN GAGCTCTTCA GACTATTGGN ATTNTCGTTC GGTCTTCTGC 180
CG NCTTGCNANG ATCTTCAT 208

Fig. 17

NUCLEOTIDE SEQUENCE OF THE REPRESENTATIVE
BREAST-TUMOR SPECIFIC cDNA B3CA2

GG GCATGGACGC AGACGCCTGA CGTTTGGCTG AAAATCTTTC ATTGATTCTG 60
AT AGGAAAATTC CCAAAGAGGG AATGTCCTGT TGCTCGCCAG TTTTNTGTT 120
GG ANAAGGCAAN GAGCTCTTCA GACTATTGGN ATTNTCGTTC GGTCTTCTGC 180
CG NCTTGCNANG ATCTTCAT 208

Fig. 18

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NUCLEOTIDE SEQUENCE OF THE REPRESENTATIVE
BREAST-TUMOR SPECIFIC cDNA B3CA3

AG GGAGCAAGGA GAAGGCATGG AGAGGCTCAN GCTGGTCCTG GCCTACGACT 60
CT GTCGCCCGGG ATGGTGGAGA ACTGAAGCGG GACCTCCTCG AGGTCCTCCG 120
TC NCCGTCCAGG AGGAGGGTCT TTCCGTGGTC TNGGAGGAGC GGGGGGAGAA 180
TC ATGGTCNACA TCCC 204

Fig. 19

NUCLEOTIDE SEQUENCE OF THE REPRESENTATIVE
BREAST-TUMOR SPECIFIC cDNA B4CA1

TC AGGAGCGGGT AGAGTGGCAC CATTGAGGGG ATATTCAAAA ATATTATTTT 60
TG ATAGTTGCTG AGTTTTTCTT TGACCCATGA GTTATATTGG AGTTTATTTT 120
CC AATCGCATGG ACATGTTAGA CTTATTTTCT GTTAATGATT NCTATTTTTA 180
GA TTTGAGAAAT TGGTINTTAT TATATCAATT TTTGGTATTT GTTGAGTTTG 240
GC TTAGTATGTG ACCA 264

Fig. 20

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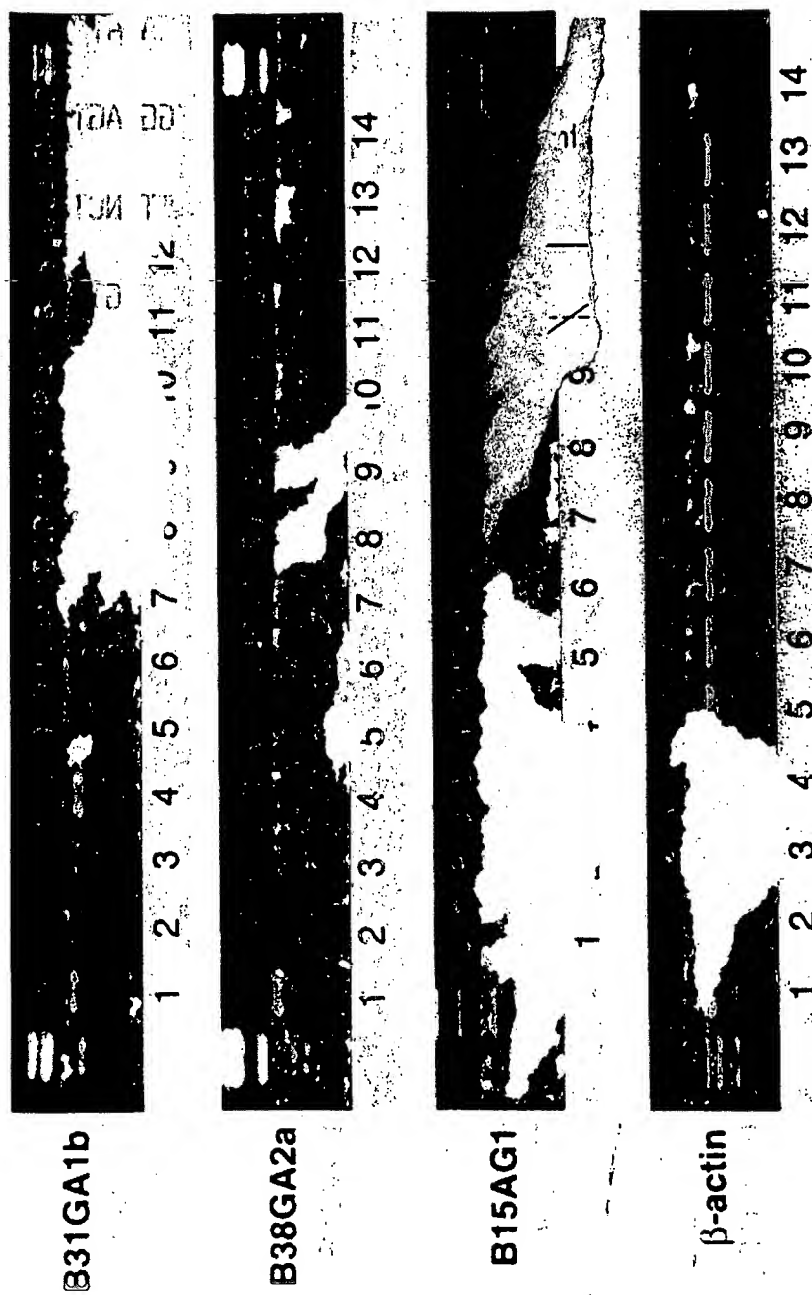


Fig. 21A

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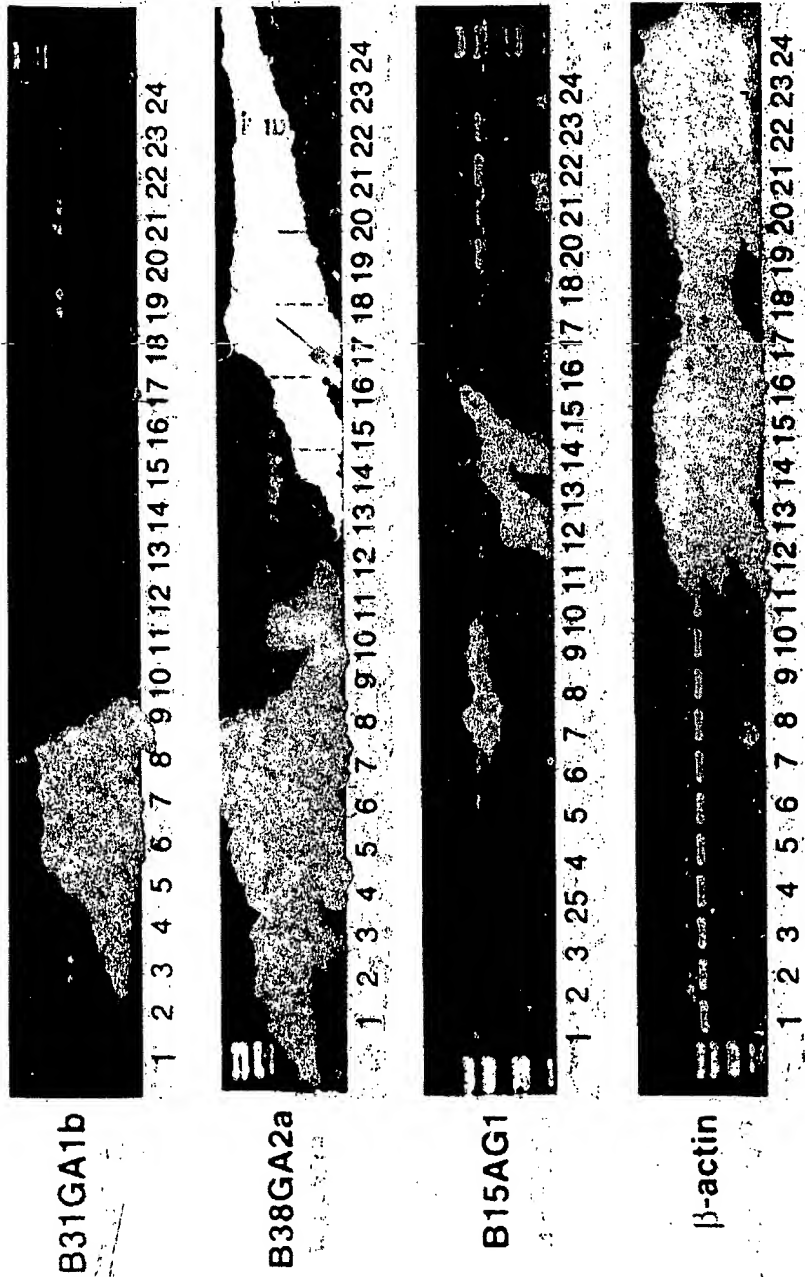


Fig. 21B

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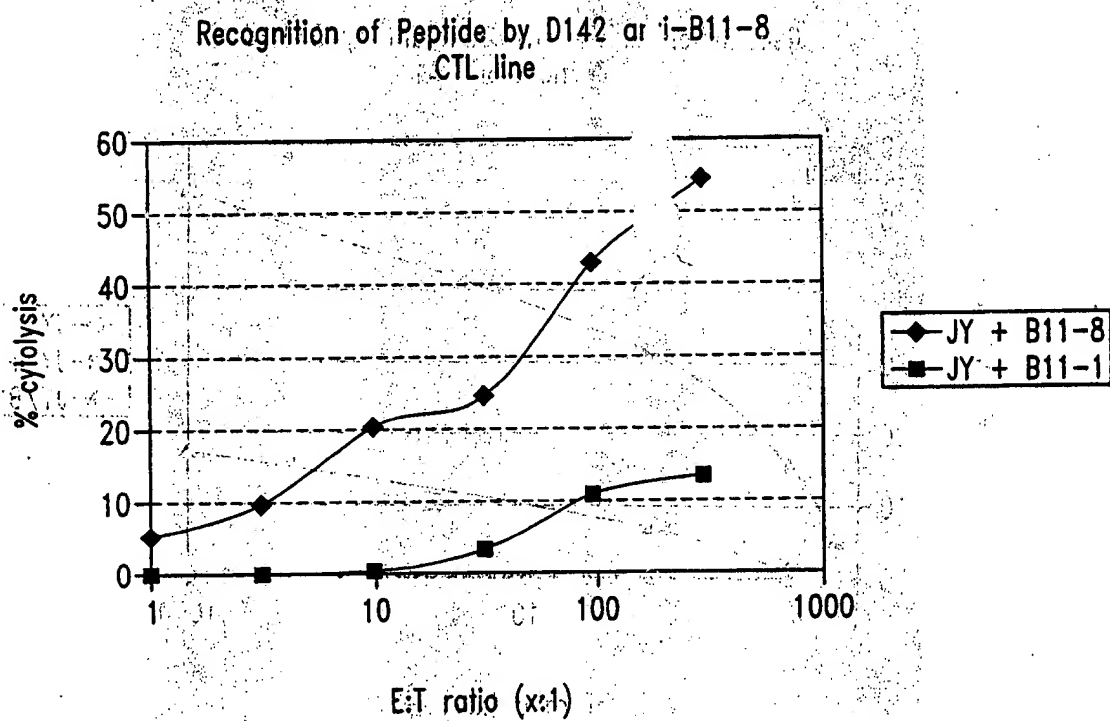


Fig. 22

Recognition of B11 Transductant by B11-8
Specific Clone A1

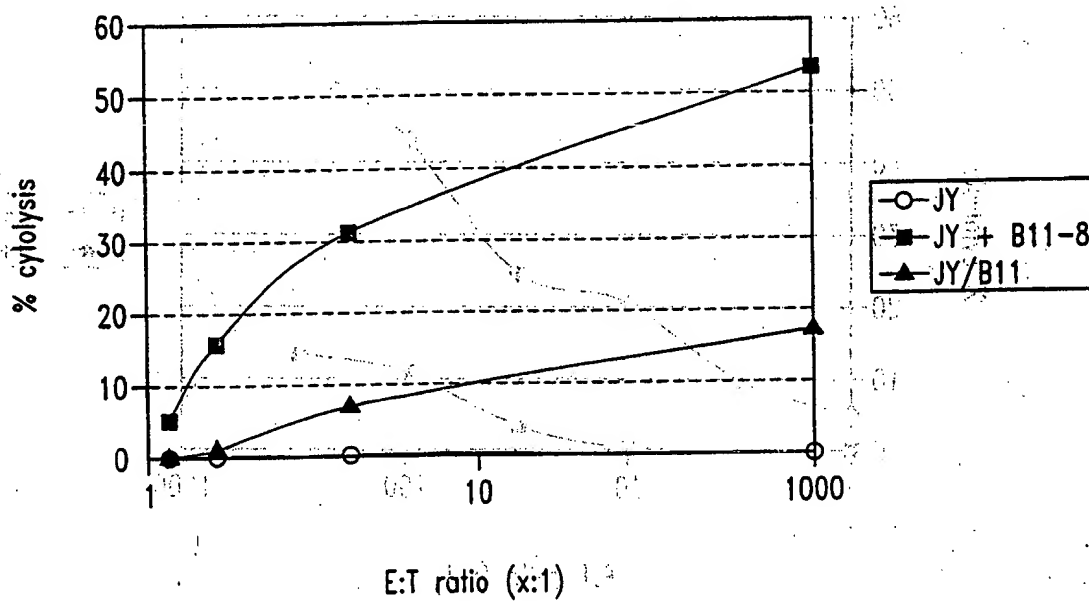


Fig. 23

(SUBSTITUTE SHEET (RULE 26)

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Recognition of Tumor Cell Lines by Clone A1

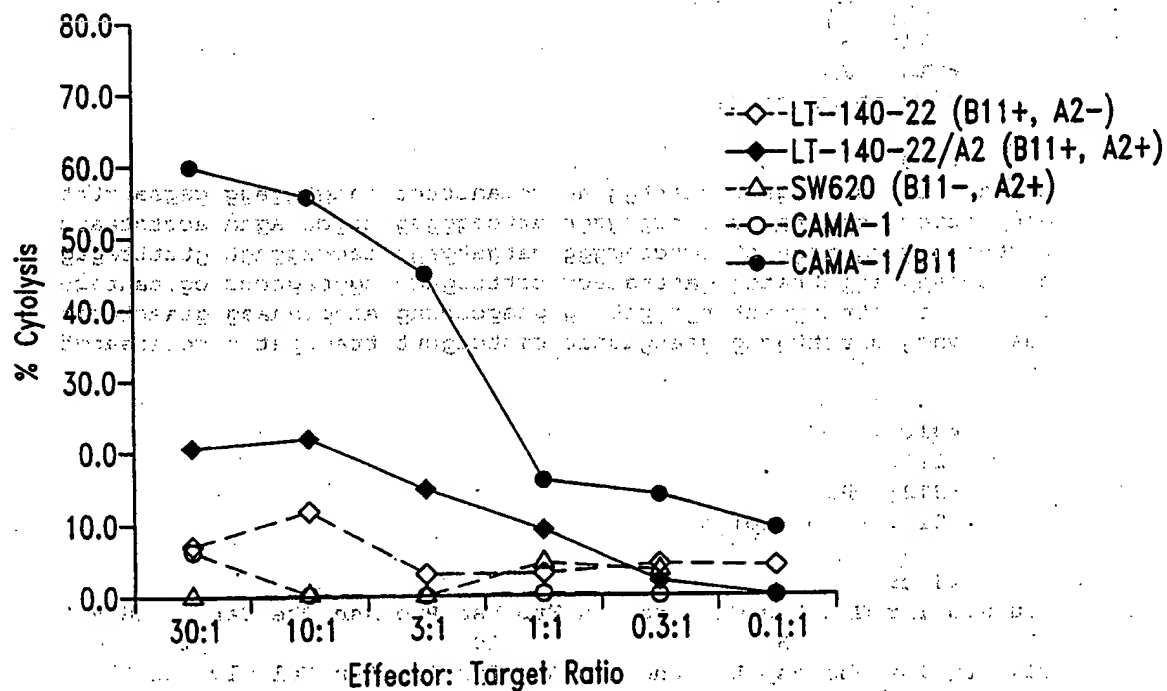


Fig 2A

SEQUENCE LISTING

<110> Corixa Corporation

<120> COMPOSITIONS AND METHODS FOR THE
TREATMENT AND DIAGNOSIS OF BREAST CANCER

<130> 210121.41926PC

<140> PCT

<141> 2000-04-07

<160> 317

<170> FastSEQ for Windows Version 3.0

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<211> 363

<212> DNA

<213> Homo sapien

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ttgtctaagg cgattgaagt cgtccagggg catgatgagt caccaggagt gtttttagag	180
cacctccagg aggcttatcg gatttacacc ccttttgacc tggcagcccc cgaaaatagc	240
catgctctta atttggcatt tgtggctcag gcagcccag atagtataag gaaactccaa	300
aaactagagg gattttgctg gaatgaatac cagtcagctt ttagagatag cctaaaaggt	360
ttt	363

<210> 2

<211> 121

<212> PRT

<213> Homo sapien

<400> 2

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20 25 30	
Gly Ala Ala Gln Lys Pro Ile Asn Leu Ser Lys Ala Ile Glu Val Val	
35 40 45	
Gln Gly His Asp Glu Ser Pro Gly Val Phe Leu Glu His Leu Gln Glu	
50 55 60	
Ala Tyr Arg Ile Tyr Thr Pro Phe Asp Leu Ala Ala Pro Glu Asn Ser	
65 70 75 80	
His Ala Leu Asn Leu Ala Phe Val Ala Gln Ala Ala Pro Asp Ser Lys	
85 90 95	
Arg Lys Leu Gln Lys Leu Glu Gly Phe Cys Trp Asn Glu Tyr Gln Ser	
100 105 110	
Ala Phe Arg Asp Ser Leu Lys Gly Phe	
115 120	

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tcttcaaagc ctaacagatc aagcagctct ccggtgcaca acctgcgccc aggtaaatgc      180
caaaaaaggt cctaaaccca gccaggcca ccgtctccaa gaaaactcac caggagaaaa      240
gtgggaaatt gactttacag aagtaaaacc acaccgggct ggggtacaaat accttctagt      300
actggtagac accttctctg gatggactga agcatttgc accaaaaacg aaactgtcaa      360
tatggttagt aagtttttac tcaatgaaat catccctcga cgtgggctgc ctgttgccat      420
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tgtagtctc cttcccttag cctacttag agttaagggt cacccttac tgggctgggt      660
tctttacctt ttgaaatcat nttnggaag gggctgccta tcttttctta actaaaaaan      720
gccatttgg caaaaatttc ncaactaatt tntacgtnc tacgtctccc caacaggtan      780
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ttcttcccc agttaactnt ttttnttaa aattcccaaa aaangaaccn cctgctggaa      900
aaacncccc ctccaanccc cggccnaagn ggaagggtcc cttgaatccc nccccncna      960
anggccegga acnttaaan tngttcngg gggtnnggc taaaagnccn atttggtaaa     1020
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 <212> DNA
 <213> Homo sapien

<220>
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<400> 4

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ttccatcat ttaaggggt taaaatcatc ttgttcagac ctcagcatat aaaatgaccc      180
atctgtagac ctcaggctcc aaccataccc caagagttgt ctggttttgt ttaaattact      240
gccaggtttc agctgcagat atccctggaa ggaatattcc agattccctg agtagtttcc      300
aggttaaaat cctataggct tcttctgttt tgaggaagag ttctgtcag agaaaaacat      360
gattttggat ttttaacttt aatgcttgtg aaacgctata aaaaaaattt tctacccta      420
gctttaaagt actgttagtg agaaattaaa attccttcag gaggattaaa ctgccatttc      480
agttacccta attccaaatg ttttgggtgt tagaatcttc tttaatgttc ttgaagaagt      540
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aaaacggant cttgtccgt tgtccangct gggaattttt ttttggcdaa tctccgtnc      660
cttgcaanaa tncgtcntcc caaaattacc ncccttttcc caccctccacc ccnnggaatt      720
acctggaatt anaggcccc ncccccccc cggttaattt gtttttgttt ttagtaaaaa      780
acgggtttcc tgttttagtt aggatggccc anntctgacc centnatcnt cccctcngc      840
cctnaatnt tnggnntang gcttaccccc ccnngnngtt tttctccat tnaaattttc      900
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tntggantct tgaatnncgg gttttccctt ttaaaccnat tttttttttn nnnccccan	960
ttttncctcc ccctntnta anggggggtt cccaanccgg gtccnccccc angtcéccaa	1020
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cnantnt	1087

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 <213> Homo sapien

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aggtaacaca catactatct cccaaatacc taccacaaag ctcaacaatt ttaaactgtt	180
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agacagaaatg tttccactcc tgatccactg tgtgggaaga agcacagaa ttacccactg	300
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naaéccacca tcccacanc tctctgtt ntgggacctg catettgtgg ctctenttnc	420
tttnggggan acntggggaa ggtaccccat ttctttgacc cccnanaaaa acccngtgg	480
ccctttgccc tgattcnctt gggocttttc tcttttccct tttgggtgtt ttaaattccc	540
aatgtcccn gaacctctc cntnctgcc aaaacctacc taaattntct netangnntt	600
ttcttgggtg tntttttcaa aggtnacctt nctgttcan ncccnacnaa aatttnttcc	660
ntatnttggc cccnaaaaaa nnnatcnnc cnaattgccc gaattggtn gggttttccct	720
nctgggggaa accctttaaa tttccccctt ggccggcccc ccttttttcc ccccttnga	780
aggcaggngg ttcttcccga actccaatt ncaacagccn tgccattgn tgaaacctt	840
ttcctaaaat taaaaaatan ccggttnngg nnggcctctt tccctccng gngggngng	900
aaantcctta cccnaaaaa ggttgcttag ccccngtcc ccactcccc nggaaaaatn	960
aacctttttn aaaaaaggaa tataantttt ccactccttn gttctcttcc	1010

<210> 6
 <211> 950
 <212> DNA
 <213> Homo sapien

<220>
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 <222> (1)..(950)
 <223> n = A,T,C or G
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ctgggattac aggcgtgcaa caccacaccc ggctaatttt gtatttttaa tagagatggg	180
gttttccctt gttggccan atggtctcna accctgacc tcnngtgatc ccccncccn	240
ngantcenna ctgctgggga tnnccgnnnn nnnctcccn ncnnnnnnnn ncnntccn	300
tnntccttnc tcnnnnnnnn cnntcnntcc ncttctene cnntntnt ntncnncnn	360
cnncnccnt ncccnccnt tcnctncnn tntccnncn nntcnncnn cnnnccntn	420
cnntacntc nttnncnnt cctctntnn cctcnncnt cctnccnt tntctctc	480
ntnnnnnct cccnnntct cctcnncn tncctcanta nccncccc nctcncnt	540
ctntttttnn cncnntctc ntncnttcn nntcnnntn cncntcncn nntntnttc	600

ccnccnnttc cttncnctn nnnntnctnn cncntcnntc ntttncctc nntcccnnc 660
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 tntcncttc nctnntnct tncntcnnc nncnntnnc tncntntnt ctnntcnnc 780
 tcnctntcn cctccnttn ctnctctcctn tntcctccc ctncctndt ctttcncc 840
 ccnntntntn tnnccnct nctnnnncn cncntttn tctctnctn nntnnccctc 900
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 <212> DNA
 <213> Homo sapien
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 <222> (1)...(1086)
 <223> n = A,T,C or G

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 agaaaaatc ttctgccttg agatgctgtt aatctgtaac cctagcccca accctgtgct 180
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 aaaagtgtt gaagataata tgcttggttaa aagtcacac cattctctaa tctcaagtac 300
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 gactgtccc cagcccgaca tccccagcc cgacatccc cagcccgaca cccgaaaagg 480
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 ctctgtctcc tgcctgtccc tgggcaataa aatgtcttgg tgtaaacc gaattgtatg 600
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 atactgtct ttaatgcacg agatgtttgt ntaattgcca tccagggcca nccctttcc 720
 ttaactttt atganacaaa aactttgttc ncttttctg cgaacctct cccctattan 780
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 aacntgtccc ggntccttn tccnccccc ctccengan aaaaaacccc gtntganggn 960
 gccccctcaa attataacct ttccnaaaca aannngttcn aaggtggtt gnttcgggtg 1020
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 ntcccc 1086

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 <211> 1177
 <212> DNA
 <213> Homo sapien
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 <221> misc_feature
 <222> (1)...(1177)
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 ctgtcaggaa ctgttggaac ctactgaac tggccgacct gatcttcaa atgtgccct 240
 aggaaagggt gatgccacc tgttcacaga cagtacccc ttctcgaga agggactacg 300
 aggggcccgt gcanctgtta ccaaggagac tnatgtgtt tgggtcagg ctttaccanc 360

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<211> 1146

<212> DNA

<213> Homo sapien

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<212> DNA

<213> Homo sapien

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taatatacct acccatcgg agagcctgag tgaggcgat caattcagcc cttttgtgct 480
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accgg 545

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<211> 196
<212> DNA
<213> Homo sapien
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ctctacgaaa aaataaaaaa atgagcctgg ttagtggaac cacaccagct gaggaggag 180
aatcagcct aggaga 196

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```

<210> 12
<211> 388
<212> DNA
<213> Homo sapien

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```

<220>
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<222> (1)...(388)
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taataaaataa ggaaaacgat gtctgtgtat agccaagtca gntatcctaa aaggagatac 180
taagtacat taaatatcag aatgtaaaac ctggaacca ggttcccagc ctgggattaa 240
actgacagca agaagactga acagtactac ttgtgaaaagc ccgaagnngc aatatgttca 300
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tactatacct cctttatagc ctaggaga 388

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```

<210> 13
<211> 337
<212> DNA
<213> Homo sapien

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<400> 13
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acaagatatg attttacat cagatgctct ttcttttctt gtttatttcc tttttatttc 180
ggttggtggg tgaatgtaa tagctttgtt tcaagagaga gttttggcag tttctgtagc 240
ttctgacact gctcatgtct ccaggcatct atttgcactt taggaggtgt cgtgggagac 300
tgagaggtct attttttcca tatttgggca actacta 337

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<210> 14
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<212> DNA

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<213> Homo sapien
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<222> (1)...(571)
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aaaatcatat ttcataattt acgctcgagg gtttttaccg gttccttttt acactcctta 180
aaacagtttt taagtctgtt ggaacaagat attttttctt tcctggcagc ttttaacatt 240
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gtttggagcg gctgctgtat atagttttaa atggtttatt gcacctcctt aagttgcact 420
tatgtggggg ggggnttttg natagaaagt ntttanteac anagtcacag ggacttttnt 480
cttttgggna ctgagctaaa aagggctgnt tttcgggttg gggcagatga agggctcacag 540
gaggccttct tcttagaggg gggaactnct

```

```

<210> 15
<211> 548
<212> DNA
<213> Homo sapien
<220>
<221> misc_feature
<222> (1)...(548)
<223> n = A,T,C or G
<400> 15

```

```

tatatattta ataacttaaa tatattttga tcacccactg ggttgataag acaatagata 60
taaaagtatt tccaaaaagc ataaaaacca agtatsatac caaaccaaat tcabactggt 120
tccccacccc gcaactgaaac ttcacctctc gaactgtctac ctaaccaaatt tctacccttc 180
aagtcttttg tgcgtgctca ctactctttt tttttttttt ttttttttgg agatggagtc 240
tggctgtgca gccagggggt ggagtacaat ggcacaacct cagctcactg naacctccgc 300
ctcccagggt catgagattc tcctgnttca gccttccag tagctgggac tacagggtgtg 360
catcaccatg cctggntaat ctpttttngt tttngggtag agatgggggt tttacatgtt 420
ggccaggntg gtntcgaact cctgacctca agtgatccac ccacctcagg ctcccaaagt 480
gctaggatta cagacatgag cactgngcc cagnctggt gcatgctcac ttctctaggg 540
aactacta 548

```

```

<210> 16
<211> 638
<212> DNA
<213> Homo sapien
<220>
<221> misc_feature
<222> (1)...(638)
<223> n = A,T,C or G
<400> 16

```

```

ttccgttatg cacatgcaga atattctatc ggtacttcag ctattactca ttttgatggc 60
gcaatccgag cctatcctca agatgagtat ttagaaagaa ttgatttagc gatagaccaa 120
gctggtaagc actctgacta cagcaaattg ttcagatgtg atggatttat gacagttgat 180

```

```

ctttggaaga gattattaag tgattatatt aaaggggaatc cattaattcc agaatatctt 240
ggtttagctc aagatgatag agaaatagaa cagaaagaga ctacaaatga agatgtatca 300
ccaactgata ttgaagagcc tatagtagaa aatgaattag ctgcatttat tagccttaca 360
catagcgatt ttcctgatga atcttatatt cagccatcga catagcatta cctgatgggc 420
aaccttacga ataatagaaa ctgggtgcgg ggctattgat gaattcatcc ncagtaaatt 480
tggatatnac aaaatataac tcgattgcat ttggatgatg gaatactaaa tctggcaaaa 540
gtaactttgg agctactagt aacctctctt tttgagatgc aaaattttct tttagggttt 600
cttattctct aacttacgga tattggagca taacggga 638

```

<210> 17

<211> 286

<212> DNA

<213> Homo sapien

<400> 17

```

actgatggat gtcgcgggag gcgaggggccc ttatctgatg ctgggtgcc tgttcgtgat 60
gtgcgcggcg attgggctgt ttatctcaaa caccgccacg gcggtgctga tggcgccat 120
tgccttagcg gcggcgaagt caatgggcgt ctacccctat ccttttgcca tgggtggggc 180
gatggcggtc tcggcggcgt ttatgacccc ggtctctctg ccggttaaca ccctgggtgt 240
tggccctggc aagtactcat ttagcgattt tgtcaaaata ggcgtg 286

```

<210> 18

<211> 262

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(262)

<223> n = A,T,C or G

<400> 18

```

tcggatcatag cagcccttc ttctcaattt catctgtcac taccctgggtg tagtatctca 60
tagccttaca tttttatagc ctctccctg gtctgtcttt tgattttctt gcctgtaate 120
catatcacac ataactgcaa gtaaacattt ctaaagtgtg gttatgtcca tgtcactct 180
gtgncaagaa atagtttcca ttaccgtctt aataaaattc ggatttgttc ttttctattn 240
tcactcttca cctatgaccg aa 262

```

<210> 19

<211> 261

<212> DNA

<213> Homo sapien

<400> 19

```

tcggatcatag caaagccagt ggtttgagct ctctactgtg taaactccta aaccaaggcc 60
atttatgata aatgggtggc ggatttttat tataaacatg taccatgca aatttctat 120
aactctgaga tatattcttc tacatttaaa caataaaaat aatctatttt taaaagccta 180
atttgcgtag ttaggtaaga gtgtttaatg agagggtata aggtataaat caccagtcaa 240
cgtttctctg cctatgaccg a 261

```

<210> 20

<211> 294

<212> DNA

<213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(294)
 <223> n = A,T,C or G
 <400> 20
 tacaacgagg cgacgtcggt aaaatcggac atgaagccac cgctgggtctt ttctgctcgag 60
 cgataggcgc cggccagcca gcggaacggt tgcgccgatg gccaagcgag caggagtctt 120
 tcggactgag tatgaatctt gttgtgaaaa tactcgccgc cttcgttcga cgacgtcgcg 180
 tcgaaatctt cganctcctt acgatcgaag tcttcgtggg cgacgatcgc ggtcagttcc 240
 gccccaccga aatcatgggt gagccggatg ctgnccccga agnctcgtt tgn 294

<210> 21

<211> 208

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(208)

<223> n = A,T,C or G

<400> 21

ttggtaaagg gcatggacgc agacgcctga cgtttggtg aaaatctttc attgattcgt 60
 atcaatgaat aggaaaattc ccaaagaggg aatgtcctgt tgctcgccag ttttttngtt 120
 gttctcatgg anaaggcaan gagctcttca gactattggn attntcgttc ggtcttctgc 180
 caactagtcg ncttgcnang atcttcat 208

<210> 22

<211> 287

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(287)

<223> n = A,T,C or G

<400> 22

nccnttgagc tgagtgattg agatntgtaa tgggtgtaag ggtgattcag ggggattagg 60
 gtggcgggtc acccggcagt gggctctccc acaggccagc aggatttggg gcagggtacgg 120
 ngtgcgcac gctcgactat atgctatggc aggcgagccg tggaaggngg atcaggtcac 180
 ggcgtggag ctttccacgg tccatgnatt gngatggctg ttctaggcgg ctgttgccaa 240
 gcgtgatggg acgctggctg gagcattgat ttctgggtgcc aaggtgg 287

<210> 23

<211> 204

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(204)

<223> n = A,T,C or G

<400> 23
ttgggtaaaag ggagcaagga gaaggcatgg agaggctcan gctggctcctg gcctacgact 60
gggccaagct gtcgccgggg atgggtggaga actgaagcgg gacctcctcg aggtcctccg 120
ncgttacttc nccgtccagg aggaggggtct ttccgtgggtc tnggaggagc ggggggagaa 180
gatnctcctc atggtcnaca tccc 204

<210> 24
<211> 264
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(264)
<223> n = A,T,C or G
<400> 24
tggattgggtc aggagcgggt agagtggcac cattgagggg atattcaaaa atattatattt 60
gtcctaataatg atagtgtgtg agtttttctt tgacctatga gttatattgg agtttatttt 120
ttaactttcc aatcgatgg acatgttaga cttattttct gttaatgatt nctattttta 180
ttaaattgga tttagaaaat tggttnttat tatatcaatt tttggtattt gttgagtttg 240
acattatagc ttagtatgtg acca 264

<210> 25
<211> 376
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(376)
<223> n = A,T,C or G
<400> 25
ttacaacgag gggaaactcc gtctctacaa aaattaaaaa attagccagg tgtgggtgggtg 60
gtcacccgca atcccagcta cttgggaggt tgagacacaa gantcaccta natgtggggag 120
gtcaaggttg catgagtcac gattgtgcca ctgcaactcca gcctgggtga cagaccgaga 180
ccctgcctca anaganaang aataggaagt tcagaaatcn tggntgtggn gccagcaat 240
ctgcatctat ncaacctctg caggcaangc tgatgcagcc tangttcaag agctgctgtt 300
tctggaggca gcagttnggg cttccatcca gtatcacggc cacactcgca cnagccatct 360
gtcctccgtn tgnac 376

<210> 26
<211> 372
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(372)
<223> n = A,T,C or G
<400> 26
ttacaacgag gggaaactcc gtctctacaa aaattaaaaa attagccagg tgtgggtgggtg 60
gtcacctgta atcccagcta cttgggcggc tgagacacaa gaaccaccta aatgtggggag 120

```

gggtcaagggtt gcatgagtc tgcgcgcgc actgcactcc agcctgggtg acagactgag 180
accctgcctc aaaagaaaa gaataggag ttcagaaacc ctgggtgtgg ngcccagcaa 240
tctgcattta aacaatccct gcaggcaatg ctgatgcagc ctaagtcca gagctgctgt 300
tctggaggca gnagtaaggg ctcccatcca gcatcacggn caacactgca aaagcacctg 360
tcctcgttgg ta 372

```

```

<210> 27
<211> 477
<212> DNA
<213> Homo sapien

```

```

<400> 27
ttctgtccac atctacaagt tttattttatt ttgtggggtt tcagggtgac taagtttttc 60
cctacattga aaagagaagt tgctaaaagg tgcacaggaa atcattttt taagtgaata 120
tgataatatg ggtccgtgct taatacaact gagacatatt tgttctctgt ttttttagag 180
tcacctctta aagtccaatc ccacaatggt gaaaaaaaaa tagaaagtat ttgttctacc 240
tttaaggaga ctgcagggat tctccttgaa aacggagtat ggaatcaatc ttaaataaat 300
atgaaattgg ttggtcttct gggataagaa attcccaact cagtgtgctg aaattcacct 360
gactttttt gggaaaaaat agtcgaaaat gtcaatttgg tccataaaat acatgttact 420
attaaaagat attaaagac aaattctttc agagctctaa gattggtgtg gacagaaa 477

```

```

<210> 28
<211> 438
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1)...(438)
<223> n = A,T,C or G

```

```

<400> 28
tctncaacct cttgantgtc aaaaaccttn taggctatct ctaaaagctg actggtatct 60
attccagcaa aatccctcta gtttttggag tttcctttta ctatctgggg ctgectgagc 120
cacaaatgcc aaattaagag catggctatt ttccgggggt gacagggtcaa aaggggtgta 180
aatccgataa gcctcctgga ggtgctctaa aaacaetctt ggtgactcat catgccctctg 240
gacgacttca atcgncttag acaagtttat aggttttctg gcagctccct gaataccacc 300
gaggagattc cgggtggaaat cgtcaaaaagt tctccctcca cttgagaaat ttgggtccca 360
attaggtccc aattgggtct ctaatcacta tctctctagc ttcctcctcc ggnctattgg 420
ttgatgtgag gttgaaga 438

```

```

<210> 29
<211> 620
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1)...(620)
<223> n = A,T,C or G

```

```

<400> 29
aagagggtac cagccccaag ccttgacaac ttccataggg tgtcaagcct gtgggtgcac 60
agaagtcaaa aattgagttt tgggatctc agcctagatt tcagaggata taaagaaaca 120
cctaacacct agatattcag acaaaaagttt actacagggg tgaagcttcc acggaaaacc 180

```

```

tctactagga aagtacagaa gagaaatgtg ggtttggagc ccccaaacag aatccccctct 240
agaacactgc ctaatgaaac tgtgagaaga tggccactgt catccagaca ccagaatgat 300
agaccacacca aaaacttatg ccatattgcc tataaaacct acagacactc aatgccagcc 360
ccatgaaaaa aaaactgaga agaagactgt nccctacaat gccaccggag cagaactgcc 420
ccaggccatg gaagcacagc tcttatatca atgtgacctg gatgttgaga catggaatcc 480
nangaaatcn ttttaanact tccacggttt aatgactgcc ctattanatt cngaacttan 540
atccnggect gtgacctctt tgctttggcc attccccctt tttggaatgg ctnttttttt 600
cccattgect tncctcttta

```

```

<210> 30
<211> 100
<212> DNA
<213> Homo sapien
<400> 30

```

```

ttacaacgag ggggtcaatg tcataaatgt cacaataaaa caatctcttc tttttttttt 60
tttttttttt tttttttttt tttttttttt tttttttttt 100

```

```

<210> 31
<211> 762
<212> DNA
<213> Homo sapien
<220>
<221> misc_feature
<222> (1)..(762)
<223> n = A,T,C or G
<400> 31

```

```

tagtctatgc gccggacaga gcagaattaa attggaagtt gccctccgga ctttctaccc 60
acactcttcc tgaaaagaga aagaaaaga gcaggaaga ggttaggatt tcattttcaa 120
gagtcagcta attaggagag cagagtttag acagcagtag gcaccccatg atacaaacca 180
tggaacaaagt ccctgttttag taactgccag acatgatcct gctcaggttt tgaaatctct 240
ctgccataaa aagatggaga gcaggagtgc catccacatc aacacgtgtc caagaaagag 300
tctcagggag acaaggggtat caaaaaacaa gattcttaat gggaaggaaa tcaaaccaaa 360
aaattagatt tttctctaca tatatataat atacagatat ttaacacatt attcagagg 420
tggtccagt ccttggggct tgagagatgg tgaaaacttt tgttccacat taacttctgc 480
tctcaaattc tgaagtatat cagaatggga caggcaatgt tttgtccac actggggcac 540
agacccaaat ggttctgtgc ccgaagaaga gaagcccga agacatgaag gatgcttaag 600
ggggggttggg aaagccaaat tgggtantatc ttttctcctt gcctgtgttc cngaagtctc 660
cnctgaagga attcttaaaa ccctttgtga ggaaatgcc ccttaccatg acaantggtc 720
ccattgcttt taggnggatg gaaacaccaa gggttttgat cc 762

```

```

<210> 32
<211> 276
<212> DNA
<213> Homo sapien
<400> 32

```

```

tagtctatgc gtgtattaac ctccccctcc tcagtaacaa ccaaagagggc aggagctgtt 60
attaccaacc ccattttaca gatgcacaa taatgacaga gaagtgaagt gacttgcgca 120
cacaaccagt aaattggcag agtcagattt gatccatgg agtctgggtc gcactttcaa 180
tcaccgaata ccctttctaa gaaacgtgtg ctgaatgagt gcatggataa atcagtgtct 240
actcaacatc ttgcctaga tatccgcgat agacta 276

```

<210> 33
 <211> 477
 <212> DNA
 <213> Homo sapien
 <400> 33
 tagtagttgc caaatatttg aaaatttacc cagaagtgat tgaaaacttt ttggaacaa 60
 aaacaaataa agccaaaagg taaaataaaa atatctttgc actctcgtta ttaactatcc 120
 ataacttttt caccgtaagc tctcctgctt gttagtgtag tgtggttata ttaaaacttt 180
 tagttattat tttttattca cttttccact agaaagtcat tattgattta gcacacatgt 240
 tgatctcatt tcattttttc tttttatagg caaaatttga tgctatgcaa caaaaatact 300
 caagcccatt atcttttttc cccccgaaat ctgaaaattg caggggacag aggggaagtta 360
 tccattataa aaattgtaaa tatgttcagt ttatgtttta aaatgcacaa aacataagaa 420
 aattgtgttt acttgagctg ctgattgtaa gcagttttat ctcaggggca actacta 477

<210> 34
 <211> 631
 <212> DNA
 <213> Homo sapien
 <400> 34
 tagtagttgc caattcagat gatcagaaat gctgctttcc tcagcattgt cttgttaaac 60
 cgcattgccat ttggaacttt ggcagtgaga agccaaaagg aagagggtgaa tgacatatat 120
 atatatatat attcaatgaa agtaaaatgt atatgctcat atactttcta gttatcagaa 180
 tgagttaaagc tttatgccat tgggctgctg catattttta tcagaagata aaagaaaatc 240
 tgggcatttt tagaatgtga tacatgtttt tttaaaactg ttaaatatta tttcgatatt 300
 tgtctaagaa coggaaatgtt cttaaaattt actaaaacag tattgtttga ggaagagaaa 360
 actgtactgt ttgccattat tacagtcgta caagtgcattg tcaagtcacc cactctctca 420
 ggcattcagta tccacctcat agctttacac attttgacgg ggaatattgc agcatctctca 480
 ggcttgacat ctgggaaagg ctcagatcca cctactgctc cttgctcgtt gatttggttt 540
 aaaatattgt gcctggtgtc acttttaagc ctcagccttg cctaaaagcc agcagagaa 600
 agaaccgcga ccattctata ggcaactact a 631

<210> 35
 <211> 578
 <212> DNA
 <213> Homo sapien
 <400> 35
 tagtagttgc catcccatat tacagaaggc tctgtatata tgacttattc ggaagtgate 60
 tgttttctct ccaaaccat ttatcgtaat ttcaccagtc ttggatcaat cttggtttcc 120
 actgattacca tgaaacctac ttggagcaga cattgcacag tttctgtggt taaaactaa 180
 aggtttattt gctaagctgt catcttatgc ttagtatttt ttttttacag tggggaattg 240
 ctgagattac attttgttat tcattagata ctttgggata acttgacact gtcttctttt 300
 tttcgctttt aattgctatc atcatgcttt tgaaacaaga acacattagt cctcaagtat 360
 tacataagct tgcttgttac gcctggtggt ttaaaggact atctttggcc tcagggtcac 420
 aagaatgggc aaagtgttct cttatgttct gtagttctca ataaaagatt gccaggggcc 480
 gggtagctgt gctgcactg taatcccagc actttgggaa gctgaggctg gcggatcatg 540
 ttagggcagg tgttcgaac cagcctgggc aactacta 578

<210> 36
 <211> 583
 <212> DNA
 <213> Homo sapien

<400> 36

tagtagttgc	ctgtaatccc	agcaactcag	gaggctgggg	caggagaatc	agttgaacct	60
gggaggcaga	agttgtaatt	agcaaagatc	gcaccattgc	acttcagcct	gggcaacaag	120
agttagattc	catctcaaaa	acaaaaaaa	gaaaaagaaa	agaaaaggaa	aaaacgtata	180
aaccagcca	aaacaaaatg	atcattcttt	taataagcaa	gactaattha	atgtgtttat	240
ttaatcaaag	cagttgaatc	ttctgagtta	ttggtgaaaa	tacccatgta	gttaatttag	300
ggttcttact	tgggtgaacg	tttgatgttc	acaggttata	aatgggttaa	caaggaaaat	360
gatgcataaa	gaatcttata	aactactaaa	aataataaaa	atataaatgg	ataggtgcta	420
tggatggagt	ttttgtgtaa	tttaaatctt	tgaagtcatt	ttggatgctc	attggttgct	480
tggtaatctc	cattaggaag	aggttatgat	atggggaaac	tgtttctgga	aattgcggaa	540
tggttctcat	ctgtaaaatg	ctagtatctc	agggcaacta	cta		583

<210> 37

<211> 716

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)... (716)

<223> n = A,T,C or G

<400> 37

gatctactag	tcaatntggat	tatatccatg	gcagctaagc	ctttctgaat	ggattctact	60
gctttcttgt	tctttaatcc	agacccttat	atatgtttat	gttcacaggc	agggcaatgt	120
ttagtgaaaa	caattctaaa	ttttttat	tgcattttca	tgctaatttc	cgtcacactc	180
cagcaggcct	cctgggagaa	taaggagaaa	tacagctaaa	gacattgtcc	ctgcttactt	240
acagccta	ggtagcaaaa	accacttcaa	taaagtaaca	ggaaaagtac	taaccaggta	300
gaatggacca	aaactgat	agaaaaatca	gaggaagaga	ggaacaaata	tttactaggt	360
cctagaatgt	acaaggcttt	ttaattacat	attttatgta	aggcctgcaa	aaaacaggtg	420
agtaatcaac	atttgtccca	ttttacatat	aaggaaaactg	aagcttaaat	tgaataattt	480
aatgcataga	ttttatagtt	agaccatgtt	caggtcccta	tggtatactt	actagctgta	540
tgaatatgag	aaaataattt	tggtattttc	ttggcatcag	tattttcatc	tgcaaaataa	600
agctaaagtt	atttagcaaa	cagtcagcat	agtgcctgat	acatagtagg	tgctccaaac	660
atgattacnc	tantatnngg	tattanaaaa	atccaatata	ggcntggata	aaaccg	716

<210> 38

<211> 688

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)... (688)

<223> n = A,T,C or G

<400> 38

ttctgtccac	atatcatccc	actttaattg	ttaatcagca	aaactttcaa	tgaaaaatca	60
tccattttta	ccaggatcac	accaggaaac	tgaagggtgta	ttttttttta	ccttaaaaaa	120
aaaaaaaaa	accaaacaaa	ccaaaacaga	ttaacagcaa	agagttctaa	aaaattttaca	180
tttctcttac	aactgtcatt	cagagaacaa	tagttcttaa	gtctgttaaa	tcttggcatt	240
aacagagaaa	cttgatgaan	agttgtactt	ggaatattgt	ggattttttt	ttttgtotaa	300
tctcccccta	ttgttttgcc	aacagtaatt	taagttttgt	tggaacatcc	cctgagttga	360
agtgtaaaca	atgtatagga	aggaatatat	gataagatga	tgcatcacat	atgcattaca	420
tgtagggacc	ttcacaactt	catgcactca	gaaacatgc	ttgaagagga	ggagaggacg	480

gccagggtc accatccagg tgccttgagg acagagaatg cagaagtggc actgttgaaa 540
 tttagaagac catgtgtgaa tggtttcagg cctgggatgt ttgccaccaa gaagtgcctc 600
 cgagaaattt ctttccatt tggataacag ggtggcttga tgggtaccgt gggtagccca 660
 acgaagaaaa tgaaattctg ccttttcc 688

<210> 39

<211> 585

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(585)

<223> n = A,T,C or G

<400> 39

tagtagttgc cgcnnaccta aaanttggaa agcatgatgt ctaggaaaca tantaaaata 60
 gggtagtgcct atgtgctaca gagagatgtt agcatttaaa gtgcatantt ttatgtattt 120
 tgacaaatgc atatnctctc ataataccaca actgattacg aagctattac aattaaaaag 180
 tttggccggg cgtgggtggc ggtggctgac gctgtgaatc ccagcatttt gggaggccga 240
 ggcacgcctga tcaagaggtc gggagttoaa gaccatcctg gataacaggg tgaaagtcga 300
 tctctactaa aaatacgaaa aaattacccc ggcgtgtgtg cgggcgcctg tagtccagc 360
 tactccggag gctgaggcag gagaatggcg tgaaccagg acacggagct tgcagtgtgc 420
 caacatcacg tcaactgccct ccagcctggg ggacaggaac aagantcccg tctctaaaaa 480
 agaaaaatac tactnatant ttcnacttta ttttaantta cacagaactn cctcttggtg 540
 ccccttacc attcatctca cccacctcct atagggcacn nctaa 585

<210> 40

<211> 475

<212> DNA

<213> Homo sapien

<400> 40

tctgtccaca ccaatcttag aagctctgaa aagaatttgt ctttaaatat cttttaatag 60
 taacatgtat tttatggacc aaattgacat tttcgactgt tttttccaaa aaagtcagg 120
 gaatttcagc aactgagtt gggaatttct tatccagaa gaccaaccaa tttcatattt 180
 atttaagatt gattccatac tccgttttca aggagaatcc ctgcagtctc cttaaaggta 240
 gaacaaatac ttcctatttt tttttccca ttgtgggatt ggactttaag aggtgactct 300
 aaaaaaacag agaacaata tgtctcagtt gtattaagca cggaccata ttatcatatt 360
 cacttaaaaa aatgatttcc tgtgcacctt ttggcaactt ctcttttcaa tgtagggaaa 420
 aacttagtca cctgaaaac ccacaaaata aataaaactt gtagatgtgg acaga 475

<210> 41

<211> 423

<212> DNA

<213> Homo sapien

<400> 41

taagagggta catcggttaa gaacgtaggc acatctagag cttagagaag tctggggtag 60
 gaaaaaaatc taagtattta taagggtata ggtaacattt aaaagtaggg ctagctgaca 120
 ttatttagaa agaacacata cggagagata agggcaagg actaagacca gaggaacact 180
 aatatttagt gatcacttcc attccttggtt aaaatagtaa cttttaagtt agcttcaagg 240
 aagatttttg gccatgatta gttgtcaaaa gtttagttct ttgggtttat attactaatt 300
 ttgttttaag atccttggtt gtgctttaat aaagtcagt tatatcaaac gctctaaaac 360
 attgtagcat gttaaatgtc acaatatact taccatttgt tgtatatggc tgtaccctct 420

cta 423

<210> 42

<211> 527

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(527)

<223> n = A,T,C or G

<400> 42

tctcctaggt taatgtgtgt gtttctgtaa aagtaaaaag ttaaaaattt taaaaataga 60

aaaaagctta tagaataaga atatgaagaa agaaaatatt tttgtacatt tgcacaatga 120

gtttatgttt taagctaagt gttattacaa aagagccaaa aagggtttta aaattaaaac 180

gtttgtaaag ttacagtacc ottatgttaa tttataattg aagaaagaaa aacttttttt 240

tataaatgta gtgtagccta agcatacagt atttataaag tctggcagtg ttcaataatg 300

tcctaggcct tcaatcacc tcaactgact acccagagca acttccagtc ctgtaagctc 360

cattcgtggt aagtgcctta tacaggtgca ccatttattt tacagtattt ttactgtacc 420

ttctctatgt ttccatatct ttccgatatac aaataccact gggtactatn gccenacagg 480

taattccagt aacacggcct gtatacgtct ggtancccta gngaaga 527

<210> 43

<211> 331

<212> DNA

<213> Homo sapien

<400> 43

tcttcaacct cgtaggacaa ctctcatatg cctgggcact atttttaggt tactaccttg 60

gctgcccttc ttaagaaaa aaaaaagaag aaaaaagaac tttccacaa gtttctcttc 120

ctctagttag aaaattagag aaatcatggt ttaatttttg tgttatttca gatcacaat 180

tcaaacactt gtaaacatta agcttctggt caatcccttg ggaagaggat tcattctgat 240

atttacggtt caaaagaagt tgtaatatg tgccttgaac acagagaacn agttattaac 300

ttctactac tattatataa taaataataa c 331

<210> 44

<211> 592

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(592)

<223> n = A,T,C or G

<400> 44

ggcttagtag ttgccaggca aaatacgtt gattctcttc aggggccacc cccaacccc 60

ctgtttgctt ctagacctat acctagacta aagtcaccagc agaccctag aggtgaggtt 120

cagagtgaac cttgaggaga tgtgctacac tagaaaagaa ctgcttgagt tttctaattt 180

atataagcag aaatctggag aagagtcata ggaatggata ttaagggtgt gagataatgg 240

cgaagggaat atagagttgg atcaggctgg acttattgat ttgaaccac taagtagaga 300

ttctgctttt gatgttgag ctcaggaggt taaaaagggt ttaaatggtt ctaatagttt 360

atttgcttgg ttagctgaaa tatggataaa agatggccca ctgtgagcaa gctggaaatg 420

cctgatctct ctcatgttaa ttagagagaa gggatccaaa agtttaggga ganttgatg 480

ctggraktgg attggtcact ttgrgaccta cccwtcccag ctggggagggt ccagaagata 540
cacccttgac caacgctttg cgaaatggat ttgtgatggc ggcaactact aa 592

<210> 45
<211> 567
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)... (567)
<223> n = A,T,C or G

<400> 45
ggcttagtag ttgccattgc gagtgcttgc tcaacgagcg ttgaaatggc eggattgtct 60
agattcaacg gatttgagtt ttaccagcaa agcgaaccaa gcgcggccca gagaattatg 120
ggttggttgg ctttgaaaag atggaaatcc tgtaggccta gtcagaaaag ctttcttgca 180
gaacagtttg ttctcgggcg aacgctcatc aagatgccca ttggaaaggc tagcgtgtat 240
ttgggagagc ctgatagcgt gtcttctgat gatgtttgtg cttggacagt gacaaaagat 300
atgcaaagca agtcggaact agacgtcaag cttegtgagc aaattatctg tagactcctac 360
ttatactgtg aggaatgata gccaaagggtg gggactttta gaetaagggtg gtttgtactc 420
gcgccgatga tcccaggcag aaagamctga tgcctagttt tatacgggca actactaagg 480
cgaattccag cacactggcg gccgttacta attggatccg anctcgggtac cagcttgatg 540
catascttga gttwtctata ntgtcnc 567

<210> 46
<211> 908
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)... (908)
<223> n = A,T,C or G

<400> 46
gagcgaaga cagagggcag ngntangng cgangaagcg gagagggcca aaaagcaacc 60
gctttccccc ggggggtgcc attcattaag gcaggtggag gacaggtttc cccatggaag 120
gcggcagggg cgcaagcaat taatgtgagt aggccattca ttagcaccog ggcttaacat 180
ttaagcttcg gggttggtatg tgggtgggaat tgtgagcgga taacaatttc acacaggaaa 240
cagctatgac catgattacg ccaagctatt taggtgacat tatagaataa ctcaagttat 300
gcatcaagct tggtagccag ttccgatcca ctagtaacgg ccgccagtgt gtggaattcg 360
gcttagtagt tgccgaccat ggagtgtctac ctaggctaga atacctgagy tccctccctag 420
cctcactcac attaaattgt atcttttcta cattagatgt cctcagcgcc ttatttctgc 480
tggacwatcg ataaattaat cctgatagga tgatagcagc agattaatta ctgagagtat 540
gttaatgtgt catccctcct atataacgta tttgcatttt aatggagcaa ttctggagat 600
aatccctgaa ggcaaaggaa tgaatcttga gggtagaana gccagaatca gtgtccagct 660
gcagttgttg gagaagggtg tattatgtat gtctcagaag tgacaacata tgggcaacta 720
ctaagccgca attccagcac actggcgggc gttactaatg gatccgagct cggtaaccaag 780
cttgatgcac agcttgagta tctatagtgt cactaaatag cotggcggtta tcatggtcac 840
agctgtttcc tgtgtgaaat tgttatccgc tcccaattcc ccccaaccata cgagcgggaa 900
cataaagta 908

<210> 47
<211> 480

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1) (480)

<223> n = A,T,C or G

<400> 47

tgccaacaag gaaagtttta aatttcccct tgaggattct tggatgatcat caaattcagt	60
ggtttttaag gttgttttct gtcaaataac tctaacttta agccaaacag tatatggaag	120
cacagataka atattacaca gataaaagag gagttgatct aaagtaraga tagttggggg	180
ctttaatttc tggaacctag gtctcccat ctctctctgt gctgagggaac ttcttggaag	240
cggggattct aaagtctctt ggaagacagt ttgaaaacca ccatgttggt ctcatgacct	300
ttatttttaa aaagtaggtg aacattttga gagagaaaag ggcttggtg agatgaagtc	360
ccccccccc cttttttttt ttttagctga aatagatacc ctatgttnaa rgaarggatt	420
attatttacc atgcaytar scacatgctc tttgatgggc nytcctstac cctccttaag	480

<210> 48

<211> 591

<212> DNA

<213> Homo sapien

<400> 48

aagaggggtac cgagtggat ttccgcttca ctagtctggt gtggctagtc ggtttcgtgg	60
tggccaacat tacgaacttc caactcaacc gttcttggac gttcaagcgg gaggaccggc	120
gaggatgggtg gctgaattc tggccttct ttgccgtggg atcggtagcc gccatcatcg	180
gtatgtttat caagatcttc tttactaacc cgacctctcc gatttacctg ccgagccgt	240
ggtttaacga ggggaggggg atccagtcac gcgagtactg gtcccagatc ttgccatcg	300
tcgtgacaat gcctatcaac ttctgtctca ataagttgtg gaccttccga acggtgaagc	360
actccgaaaa cgccgggtgg ctgctgtgct gtgactccca aaatcttgat aacaacaagg	420
taaccgaatc gcgctaagga acccggcat ctccgggtact ctgcataatg gtaccctta	480
agccgaattc cagcacactg gcggccgtta ctaattggat ccgaactccg taaccaagcc	540
tgatgcgttaa cttgagttat tctatagtgt ccctaaaata acctggcggt a	591

<210> 49

<211> 454

<212> DNA

<213> Homo sapien

<400> 49

aagaggggtac ctgccttgaa atttaaatgt ctaaggaaar tgggagatga ttaagagttg	60
gtgtggcyta gtcacacca aatgtattta ttacatcctg ctcttttcta gttgacagga	120
aagaaagctg ctgtggggaa aggagggata aatactgaag ggatttacta aacaatgtc	180
catcacagag ttttctttt ttttttttg agacagagtc ttgctctgtc acccaggctg	240
gaatgaagwg gtatgatctc agttgaatgc aacctctacc tcctagggtc aagcgattct	300
catgcctcag cctcctgagc agctgggact ataggcgcat gctatcatgc caggctaatt	360
tttatatttt tattagagac ggggtgttgc catgttggcc aggcaggtct cgaactcctg	420
ggcctcagat gatctgcccc accgtaccct cttta	454

<210> 50

<211> 463

<212> DNA

<213> Homo sapien

<400> 50

aagaggggtac caaaaaaaag aaaaaggaaa aaaagaaaaa caacttggtat aaggctttct 60
gctgcataca gctttttttt tttaaataaa tgggtgccaac aaatgttttt gcattcacac 120
caattgctgg ttttgaaatc gtactcttca aagggtatttg tgcagatcaa tccaatagt 180
atgccccgta ggttttgtgg actgcccacg ttgtctacct tctcatgtag gagccattga 240
gagactgttt ggacatgcct gtgttcatgt agccgtgatg tccggggggc gtgtacatca 300
tgttaccgtg ggggtggggc tgcattggct gctgggcata tggctgggtg cccatcatgc 360
ccatctgcct ctgcataggg tattggggcg tttgatccat atagccatga ttgctgtggt 420
agccactggt catcattggc tgggacatgc tgttaccctc tta 463

<210> 51

<211> 399

<212> DNA

<213> Homo sapien

<400> 51

cttcaacctc ccaagtgtct gggattacag gactgagcca ccacgtcag cctaagcctc 60
tttttcaacta ccctctaagc gatctaccac agtgatgagg ggctaaagag cagtgcatt 120
tgattacaat aatggaactt agatttatta attaacaatt tttccttagc atgttggttc 180
cataattatt aagagtatgg acttacttag aaatgagctt tcattttaag aatttcattc 240
ttgaccttct ctattagtct gagcagtatg acactatacg tattttattt aactaaccta 300
ccttgagcta ttacttttta aaaggctata tacatgaatg tgtattgtca actgtaaaagc 360
ccacagtat ttaattatat catgatgtct ttgaggttg 399

<210> 52

<211> 392

<212> DNA

<213> Homo sapien

<400> 52

cttcaacctc aatcaacctt ggtaattgat aaaatcatca ctttaacttc tgatataatg 60
gcaataatta tctgagaaaa aaaagtgggtg aaagattaaa cttgcatttc tctcagaatc 120
ttgaaggata tttgaataat tcaaaagcgg aatcagtagt atcagccgaa gaaactcact 180
tagctagaac gttggaccca tggatctaag tccctgcctt tccactaacc agctgatttg 240
ttttgtgtaa acctctaca cgcttgggtt tggctgcctc atttgtcaaa gtaaaggctg 300
aaataggaag ataataaacc gtgtcttttt ggtctctttt ccatccatta ctctgatttt 360
acaaagaggc ctgtattccc ctggtgaggt tg 392

<210> 53

<211> 179

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(179)

<223> n = A,T,C or G

<400> 53

ttcgggtgat gcctctcag gctacagtga agactggatt acagaaaggt gccagcgaga 60
tttcagattc ctgtaaacct ctaagaaaaa ggagtcgcgc ctcaactgat gtagaatga 120
ctagttcagc atacnagac acntctgact ccgattctag aggactgagt gacctgcan 179

<210> 54

<211> 112

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(112)

<223> n=A,T,C,G

<400> 54
 ttcggtgat gctcctcag gctacatcat natagaagca aagtagaana atcnngtttg 60
 ggcattttcc cacanacaaa attcaaatga ntggaagaaa ttggganagt at 112

<210> 55

<211> 225

<212> DNA

<213> Homo sapien

<400> 55

tgagcttcg cttctgacaa ctcaatagat aatcaaagga caactttaac agggattcac 60
 aaaggagtat atccaaatgc caataaacat ataaaangga attcagcttc atcatcatca 120
 gaagwatgca aattaaaacc ataatgagaa accactatgt cccactagaa tagataaaat 180
 cttaaaagac tggtaaaacc aagtgttgg aaggcaagag gagca 225

<210> 56

<211> 175

<212> DNA

<213> Homo sapien

<400> 56

gctcctcttg ccttaccac acattctcaa aaacctgtta gactcctaag cattctcctg 60
 ttagtattgg gattttaccc ctgtcctata aagatgttat gtacaaaat tgaagtggag 120
 ggccataccc tgagggaggg gagggatctc tagtgttgtc agaagcggaa gctca 175

<210> 57

<211> 223

<212> DNA

<213> Homo sapien

<400> 57

agccatttac caccatgga tgaatggatt ttgtaattct agctgttgta ttttgtgaat 60
 ttgttaattt tgttgttttt ctgtgaaaca catacattgg atatgggagg taaaggagtg 120
 tccagttgc tctgtgtcac tccctttata gccattactg tcttgtttct tgtaactcag 180
 gttaggtttt ggtctctctt gctccactgc aaaaaaaaaa aaa 223

<210> 58

<211> 211

<212> DNA

<213> Homo sapien

<400> 58

gttcgaaggt gaactgttag gtagcggatc tcacaactgg ggaactgtca aagacgaatt 60
 aactgacttg gatcaatcaa atgtgactga ggaacacct gaaggtgaag aacatcatcc 120
 agtggcagac actgaaaata aggagaatga agttgaagag gtaaaagagg aggttccaaa 180
 agagatgact ttggatgggt ggtaaatggc t 211

<210> 59
<211> 208
<212> DNA
<213> Homo sapien

<400> 59
gtctctcttg ccttaccac tttgcaccca tcatcaacca tgtggcagg tttgcagccc 60
aggctgcaca tcaggggact gctctgcaat acttcatgct gttgctgctg actgatgggtg
120ctgtgacgga tgtggaagcc acacgtgagg ctgtgggtgctg tgcctcgaac ctgcccattg
180
cagtgatcat tatgggtggt aaatggct 208

<210> 60
<211> 171
<212> DNA
<213> Homo sapien

<400> 60
agccatttac caccataact aaattctagt tcaaaactcca acttcttcag taaaacatct 60
aaccactgac accagttggc aatagcttct tccttcttta acctcttaga gtatttatgg 120
tcaatgccac acatttctgc aactgaataa agttggtaag gcaagaggag c 171

<210> 61
<211> 134
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature

<222> (1)-(134) G...
<223> n=A,T,C or G

<400> 61

cggtgatgc ctctcaggc tttggtgtgt ccactcnact cactggcctc ttctccagca 60
actggtgaan atgtctcan gaaaancnc acacgcnct caggggtggg tgggaancat 120
canaatcatc nggc 134

<210> 62
<211> 145
<212> DNA
<213> Homo sapien

<400> 62
agaggtgaca tatgcaacag tatataaagg aagaagtga ctgagaggaa cttcatcaag 60
gccatttaat caataagtga tagagtcaag gctcaaccca ggtgtgacgg attccaggtc 120
ccaagctcct tactggtacc ctctt 145

<210> 63
<211> 297
<212> DNA
<213> Homo sapien

<400> 63
tgcaactgaga ggaattcaaa gggtttatgc caaagaacaa accagtcctc tgcagcctaa 60
ctcatttggt tttgggctgc gaagccatgt agaggcgat caggcagtag atggtccttc 120

ccacagtcag cgccatggtg gtccggtaaa gcatttggtc aggcaggcct cgtttcaggt 180
 agacggggcac acatcagctt tctggaaaaa cttttgtagc tctggagctt tctttttccc 240
 agcataatca taccatgtgg aatcggaggt cagtttagtt ggtaaggcaa gaggagc 297

<210> 64

<211> 300

<212> DNA

<213> Homo sapien

<400> 64

gcactgagag gaacttccaa tactatgttg aataggagtg gtgagagagg gcatecttgt 60
 cttgtgccgg ttttcaaagg gaatgcttcc agcttttgcc cattcagtat aatattaaag 120
 aatgttttac cattttctgt cttgcctgtt tttctgtgtt tttgttggtc tcttcattct 180
 ccatttttag gcctttacat gtttaggaata ttttctttt aatgatactt caectttggt 240
 atcttttgtg agactctact catagtgtga taagcactgg gttggttaagg caagaggagc 300

<210> 65

<211> 203

<212> DNA

<213> Homo sapien

<400> 65

gctcctcttg ccttaccac tcacccagta tgtcagcaat tttatcrgct ttacctaaga 60
 aacagcctgt atccaaacac ttaacacact cacctgaaaa gttcaggcaa caatcgctt 120
 ctcatgggtc tctctgtctc agttctgaac ctttctcttt tcttagaaca tgcatttarg 180
 tcatagaag ttcctctcag tgc 203

<210> 66

<211> 344

<212> DNA

<213> Homo sapien

<400> 66

tacggggacc cctgcattga gaaagcgaga ctactctga agctgaaatg ctgttgccct 60
 tgcagtgtg gtagcaggag ttctgtgctt tgtgggctaa ggctcctgga tgaccctga 120
 catggagaag gcagagttgt gtgcccttc tcatggcctc gtcaaggcat catggactgc 180
 cacacacaaa atgccgtttt tattaacgac atgaaattga aggagagaac acaattcact 240
 gatgtggtc gtaaccatgg atatggtcac atacagaggt gtgattatgt aaaggttat 300
 tccaccacc tcatgtggaa actagcctca atgcaggggt ccca 344

<210> 67

<211> 157

<212> DNA

<213> Homo sapien

<400> 67

gcactgagag gaacttcgta gggaggttga actggtgctt gaggaggggg aacaacaggg 60
 taaccagact gatagcatt ggatggataa tatgggtggtt gaggagggac actacttata 120
 gcagaggggtt gtgtatagcc tgaggaggca tcacccg 157

<210> 68

<211> 137

<212> DNA

<213> Homo sapien

<400> 68
gcactgagag gaacttctag aaagtgaag tctagacata aaataaaata aaaatttaaa 60
actcaggaga gacagccag cacggtggt cacgctgta atccagaac ttggggagcc 120
tgaggaggca tcacccg 137

<210> 69
<211> 137
<212> DNA
<213> Homo sapien

<400> 69
cgggtgatgc ctcctcaggc tgtattttga agactatcga ctggacttot tatcaactga 60
agaatccgtt aaaaatacca gttgtattat ttctacctgt caaaatccat ttcaaatgtt 120
gaagttcctc ttcagtgc 137

<210> 70
<211> 220
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(220)
<223> n = A,T,C or G

<400> 70
agcatgttga gccagacac gcaatctgaa tgagtgtgca cctcaagtaa atgtctacac 60
gctgcctggt ctgacatggc acaccatcnc gtggagggca casctctgct cngcctacwa 120
cgagggcant ctcatwgaca ggttcacccc accaaactgc aagaggctca nnaagtgactr 180
ccagggtmya sggacmasgg tgggaytyca ycacwcactt 220

<210> 71
<211> 353
<212> DNA
<213> Homo sapien
<220>
<221> misc_feature
<222> (1)...(353)
<223> n = A,T,C or G

<400> 71
cgtaggggtc tctatccact gctaaacat acacctgggt aaacagggac catttaacat 60
tccanctaa atatgccaag tgacttcaca tgtttatctt aaagatgtcc aaaacgcaac 120
tgattttctc ccctaaacct gtgatggtgg gatgattaan cctgagtggc ctacagcaag 180
ttaagtcaa ggtgctaaat gaangtgacc tgagatacag catctacaag gcagtacctc 240
tcaacncagg gcaactttgc ttctcanagg gcatttagca gtgtctgaag taatttctgt 300
attacaactc acggggcggg gggggaatat ctantggana gnagacoccta acg 353

<210> 72
<211> 343
<212> DNA
<213> Homo sapien

<400> 72

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gcactgagag gaacttccaa tacyatkac agagtgaaca rgcarccyac agaacaggag      60
aaaatgttyg caatctctcc atctgacaaa aggctaatat ccagawtcta awaggaaactt    120
aaacaaattt atgagaaaag aacaracaac ctcaawcaaaa agtgggtgaa ggawatgcta    180
aaargaagac atytattcag ccagtaaaca yatgaaaaaa aggtcatsa tcactgawca    240
ttagagaaat gcaaatcaaa accacaatga gataccatct yayrccagtt agaayggtga    300
tcattaaaar stcaggaaac aacagatgct ggacaagggtg tca                      343

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<210> 73
<211> 321
<212> DNA
<213> Homo sapien

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<220>
<221> misc_feature

```

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<222> (1)..(321)

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<223> n = A,T,C or G

```

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<400> 73

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```

gcactgagag gaacttcaga gagagagaga gagttccacc ctgtacttgg ggagagaaac      60
agaagggtgag aaagtctttg gttctgaagc agcttctaag atcttttcat ttgcttcatt    120
tcaaagttcc catgctgcca aagtgccatc ctttggggta ctgttttctg agctccagtg    180
ataactcatt tatacaaggg agataccagc aaaaaaagtg agcaaactct aaaaaggtgg    240
cttgagttca gccttaaata ccatcttgaa atgacacaga gaaagaanga tgttgggtgg    300
gagtggatag agaccctaac g                                              321

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<210> 74
<211> 321
<212> DNA
<213> Homo sapien

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<400> 74

```

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gcactgagag gaacttcaga gagagagaga gagttccacc ctgtacttgg ggagagaaac      60
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tcaaagttcc catgctgcca aagtgccatc ctttggggta ctgttttctg agctccagtg    180
ataactcatt tatacaaggg agataccagc aaaaaaagtg agcaaactct aaaaaggtgg    240
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agtcagataa ccttagcttc ctcatatgca aaatgagaat gaaaagtact catcgctgaa    180
tttgttttgag gattagaaaa acatctggca tgcagtagaa attcaattag tattcatttt    240
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ttgccatggg ggtttgctgc acccatcagt ccacatctca cattaggtat ttctcctaatt 180
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<212> DNA

<213> Homo sapien

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<212> DNA

<213> Homo sapien

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ccccagtgc agctaggatg tgcattctcc agccatcaag agactgagtc aagttgttcc 180
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gattttttta aatttatatt gtaaataatg tgtgtgtgtg tgtgtgtata tataatatata 360
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<212> DNA

<213> Homo sapien

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<211> 318

<212> DNA

<213> Homo sapien

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 caataaatat taacacagtc tacatttatt tggatgaatat tgcatactct ctgtactgaa 240
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 tatgattgcgc atagacta 318

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<211> 338

<212> DNA

<213> Homo sapien

<400> 82

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 cctctacata ttaccacaa cacaatgggg ctgactcacc caccacatta acaacataaa 240
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<211> 111

<212> DNA

<213> Homo sapien

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<212> DNA

<213> Homo sapien

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 tgagggtgat tcacgagttg cggacaactc ctttgatgcc aagcgaggtg cagccggaga 180
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Gly Ile

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Val Gln Gly His Asp Glu
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<210> 133
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<220>
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His Leu Gln Glu Ala Tyr Arg Ile Tyr

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 <400> 140

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 <213> Homo sapien
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<213> Homo sapien

<400> 143

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<210> 144

<211> 224

<212> DNA

<213> Homo sapien

<400> 144

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<210> 145

<211> 111

<212> DNA

<213> Homo sapien

<400> 145

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<210> 146

<211> 585

<212> DNA

<213> Homo sapien

<400> 146

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<210> 147

<211> 579

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(579)
<223> n = A,T,C or G

<400> 147

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<210> 148

<211> 249

<212> DNA

<213> Homo sapien

<400> 148

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<210> 149

<211> 255

<212> DNA

<213> Homo sapien

<400> 149

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<210> 150

<211> 318

<212> DNA

<213> Homo sapien

<400> 150

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<210> 151

<211> 323

<212> DNA

<213> Homo sapien
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 <223> n = A,T,C or G

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<210> 152
 <211> 311
 <212> DNA
 <213> Homo sapien

<400> 152
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<210> 153
 <211> 332
 <212> DNA
 <213> Homo sapien

<400> 153
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<210> 154
 <211> 345
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)... (345)
 <223> n = A,T,C or G

<400> 154
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<210> 155

<211> 295

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(295)

<223> n = A,T,C or G

<400> 155

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<210> 156

<211> 406

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(406)

<223> n = A,T,C or G

<400> 156

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<210> 157

<211> 208

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(208)

<223> n = A,T,C or G

<400> 157

tgacgcttgg	ccacttgaca	cactaaaggg	tggtactcat	cactttcttc	tctcctcggt	60
ggcatgtgag	tgcatttatt	cacttggcac	tcatttgitt	ggcagtgact	gtaahccana	120
tctgatgcat	acaccagctt	gtaaattgaa	taaagtcttc	taatactatg	tgctcacaat	180
anggtanggg	tgaggagaag	gggagaga				208

<210> 158
 <211> 547
 <212> DNA
 <213> Homo sapien

 <220>
 <221> misc_feature
 <222> (1)...(547)
 <223> n = A,T,C or G

<400> 158
 cttcaacctc cttcaacctc cttcaacctc ctggattcaa acaatcatcc cacctcagac 60
 tccttagtag ctgagactac agactcacgc cactacatct ggctaaattt ttgtagagat 120
 agggtttcat catgttgccc tggctggctc caaactcctg acctcaagca atgtgcccac 180
 ctcagcctcc caaagtgtgt ggattacagg cataagccac catgccagc ccatntttta 240
 tctttcctac cacattctta ccacactttc ttttatgttt agatacataa atgcttacca 300
 ttatgataca attgcccaca gtattaagac agtaacatgc tgcacagggt ttagccttag 360
 gaacagtagg caataccaca tagcttaggt gtgtggtaga ctataccatc taggtttgtg 420
 taagttacac tttatgtgtt ttacacaatg acaaaacat ctaatgatgc atttctcaga 480
 atgtatcctt gtcagtaagc tatgatgtac agggaaact gcccaaggac acagatatgt 540
 tacctgt 547

<210> 159
 <211> 203
 <212> DNA
 <213> Homo sapien

<400> 159
 gtcctcttgc ccttaccaac tcacccagta tgtcagcaat tttatcrgct ttacctacga 60
 aacagcctgt atccaaacac ttaacacact cacctgaaaa gtccaggcaa caatgcctt 120
 ctcatgggtc tctctgtccc agttctgaac ctttctcttt tcctagaaca tgcattttarg 180
 tcgatagaag ttctctcag tgc 203

<210> 160
 <211> 402
 <212> DNA
 <213> Homo sapien

<400> 160
 tgtaagtgcg gcagtgtgat ggggtggaaca ggggttgaag cagtaattgc aaactgtatt 60
 taacaataa taataatatt tagcatttat agagcacttt atatcttcaa agtacttgca 120
 aacattayct aattaaatac cctctctgat tataatctgg atacaaatgc acttaaaactc 180
 aggacagggt catgagaraa gtatgcattt gaaagttggt gctagctatg ctttaaaaaac 240
 ctatacaatg atgggraagt tagagttcag attctgttgg actgtttttg tgcatttcag 300
 ttcagcctga tggcagaatt agatcatatc tgcactcgat gactytgctt gataacttat 360
 cactgaaatc tgagtgttga tcatcacact gctcgactta ca 402

<210> 161
 <211> 193
 <212> DNA
 <213> Homo sapien

<400> 161
 agcatgttga gccagacac tgaccaggag aaaaaccaac caatagaaac acgccagac 60

actgaccagg agaaaaacca accaataaaa acaggccccg acataagaca aataataaaa 120
 ttagcggaca aggacatgaa aacagctatt gtaagagcgg atatatgtgt gtgtgtcttg 180
 gctcaacatg cta 193

<210> 162
 <211> 147
 <212> DNA
 <213> Homo sapien

<400> 162
 tgttgagccc agacactgac caggagaaaa accaaccaat aaaaacaggc ccggacataa 60
 gacaaataat aaaattagcg gacaaggaca tgaaaacagc tattgtaaga gcggatatag 120
 tgggtgtgtgt ctgggctcaa catgeta 147

<210> 163
 <211> 294
 <212> DNA
 <213> Homo sapien

<400> 163
 tagcatgttg agcccagaca caaatctttc ctttaagcaat aaatcatttc tgcatatgtt 60
 tttaaaacca cagctaagcc atgattatcc aaaaggacta ttgtattggg tattttgatt 120
 tgggttctta tctccctcac attatcttca tttctatcat tgacctotta tcccagagac 180
 tctcaaactt ttatgttata caaatcacat tctgtctcaa aaaatatctc acccaettct 240
 cttctgtttc tgcgtgtgta tgtgtgtgtg tgtgtgtctg ggctcaacat gcta 294

<210> 164
 <211> 412
 <212> DNA
 <213> Homo sapien
 <220>
 <221> misc_feature
 <222> (1)...(412)
 <223> n = A,T,C or G

<400> 164
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 cacctggctg caagtgcgcc agagccgccc tgactacgtg ctgctgtggg gctggggcgt 120
 gatgaactcc accgccctga aggaagccca gccaccgga tcccccgcg acagatgta 180
 cggcgtgtgg tgggccggtg cggagccga tgtgctgac gtgggcaag gcgccaaggg 240
 ctacaacgcg ctggctctga acggctacgg cagcagtcac aaggtgatcc angacatcct 300
 gaaacacgtg cagacaagg gccagggcac ggggcccaca gacgaagtgg gctcgtgtgt 360
 gtacaccgcg gccgtgatca tccagatgct ggacaaggtg tcaatcacta at 412

<210> 165
 <211> 361
 <212> DNA
 <213> Homo sapien

<400> 165
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 gaaggcaaag gagaadaggc attgtatggc aagaaaggaa gaaagagaga ggggagaaag 120
 gtgctaaggt cttttcaaca accagtctt gatggaactg agagtaagag ctcaaggcca 180
 ggtgtgtgta ctccaaccag taatcccaac attttaggag gctgaggcag gcagatgtct 240

tgaccccatg agtttgtgac cagcctgaac aacatcatga gactccatct ctacaataat 300
 tacaaaaatt aatcaggcat tgtggtatgc cctgtagtcc cagatgctgg acaagggtgc 360
 a 361

<210> 166
 <211> 427
 <212> DNA
 <213> Homo sapien
 <400> 156
 ctwgactgact catgtcccct acacccaact atcttctcca ggtggccagg catgatagaa 60
 tctgatcctg acttagggga atattttctt tttacttccc atcttgatcc cctgccggtg 120
 agtttctctg ttcagggtta gaaaggagct caggccaaag taatgaacaa atccatccctc 180
 acagacgtac agaataagag aacwtggacw tagccagcag aacmcaaktg aaamcagaac 240
 mettamctag gatracaamc merraratar ktgcycmcmc wtataataga aaccaaaactt 300
 gtatctaatc aaatattttat ccacygtcag ggcatttagt gttttgataa atacgctttg 360
 gctaggatcc ctgagggttag aatggaaraa caattgcamc gagggtaggg gacatgagtc 420
 aktctaa 427

<210> 167
 <211> 500
 <212> DNA
 <213> Homo sapien
 <220> misc_feature
 <221> (1) ... (500)
 <223> n = A,T,C or G

<400> 167
 aacgtcgcat gctcccgcc gccatggccg cgggatagac tgactcatgt cccctaagat 60
 agaggagaca cctgctaggt gtaaggagaa gatgggttagg tctacggagg ctccagggtg 120
 ggagtagttc cctgctaagg gagggtagac tgttcaacct gttcctgctc cggcctccac 180
 tatagcagat gcgagcagga gtaggagaga gggaggttaag agtcagaagc ttatgttgtt 240
 tatgcgggga aacgcrtat cgggggcagc cragttatta ggggacntr tagwyartcw 300
 agntagcatc caaagcngg gagttntccc atatgggttg accctgcaggc ggccgcatta 360
 gtgattagca tgtgagccc agacacgcac agcaacaagg acctaaactc agatcctgtg 420
 ctgattactt aacatgaatt attgtattt tttacaact ttgagttatg aggcatatta 480
 ttaggctcat attacctgga 500

<210> 168
 <211> 358
 <212> DNA
 <213> Homo sapien

<400> 168
 ttcacgcctc ggtgactcaa gcctgtaatc ccagaacttt gggaggccga ggggagcaga 60
 tcacctgagg ttgggagttt gagaccagcc tggccaacat ggtgacaacc cgtctctgct 120
 aaaaaatacaa aaattagcca agcatggttg catgcacttg taatcccagc tactcgggag 180
 gctgaggcag gagaatcact tgaggccagg aggcagaggt tgcagtgagg cagagggtga 240
 gatcatgcca ctgcactcca gcctgggcaa cagagtaaga ctccatctca aaaaaaaaaa 300
 aaaaaaagaa tgatcagagc cacaatatca gaaaaccttg agtcaccgag cgatgaaa 358

<210> 169
 <211> 1265

<212> DNA
<213> Homo sapien

<400> 169

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aacatgtatt ttatggacca aattgacatt ttcgactatt ttttccaaa aaaagtcagg 120
tgaatttcag cacactgagt tgggaatttc ttatcccaga agwccgcacg agcaatttca 180
tatttattta agattgattc catactccgt tttcaaggag aatccctgca gtctccttaa 240
aggtagaaca aatactttct attttttttt caccattgtg ggattggact ttaagagggtg 300
actctaaaaa aacagagaac aaatatgtct cagttgtatt aagcacggac ccatattatc 360
atattcactt aaaaaaatga tttcctgtgc accctttggc aaettctctt tccaatgtag 420
ggaaaaactt agtcaccctg aaaaccaca aaataaataa aacttgtaga tgtgggcaga 480
argtttgggg gtggacattg tatgtgttta aattaaacco tgtatcactg agaagctgtt 540
gtatgggtca gagaaaatga atgcttagaa gctgttcaca tcttcaagag cagaagcaaa 600
ccacatgtct cagctatatt attatttatt ttttatgcac aaagtgaata atttctcttg 660
tattaatttc caaagggttt taccctctat ttaaatgctt tgaaaaacag tgcattgaca 720
atgggttgat atttttcttt aaaagaaaaa tataattatg aaagccaaga taatctgaag 780
cctgttttat tttaaaactt tttatgttct gtggttgatg ttgtttgttt gtttgtttct 840
attttgttg ttttttactt tgtttttgt tttgtttgt tttggtttdg catactacat 900
gcagtttctt taaccaatgt ctgtttggct aatgtaatta aagttgttaa tttatatgag 960
tgcatttcaa ctatgtcaat ggtttcttaa tatttattgt gtagaagtac tggtaatttt 1020
tttatttaca atatgtttta agagataaca gtttgatatt ttttcatgtg tttatatgag 1080
aagttattta tttctatggc attccagcgg atattttggt gtttgcaggg catgcagtca 1140
atattttgta cagttagtgg acagtattca gcaacgcctg atagcttctt tggccttatg 1200
ttaaataaaa agacctgttt gggatgtaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 1260
aaaaa
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<210> 170

<211> 383

<212> DNA

<213> Homo sapien

<400> 170

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tgtaagtcca gcagtgtgat gacgatattc tttttattaa ttttggttaatt gaacaaatga 60
tctgtgatac tgatcctgag ctaggaggcg ctgttcagtt aatgggaactt ctctgactc 120
taattgatcc agagaacatg ctggctacaa ctatataaac cgaaaaaagt gaatttctaa 180
attttttcta caaccattgt atgcatgttc tccacagcact acttttgacc attacttcag 240
aagacaaatg tgaaaaaggat aatatagttg gatcaaacaa aaacaadaca atttgtcccg 300
ataattatca aacagcacag ctacttgctt taattttaga gttactcaca ttttgtgtgg 360
aacatcacac tgctcgactt aca 383
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<210> 171

<211> 383

<212> DNA

<213> Homo sapien

<400> 171

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tgggcacctt caatatcgca agttaaaaat aatgttgagt ttattatact tttgacgtgt 60
ttagctcaac aggttgaagg catgtaadaga atgtggactt ctgaggaatt ttcttttaaa 120
aagaacataa tgaagttaaca ttttaattac tcaaggacta cttttggttg aagtttataa 180
tctagatacc tctacttttt gtttttgetg ttgcagagtt cacaagacc ttcagcaatt 240
tacagggtaa aatcgttgaa gtagtggagg tgaactgaa atttaaaatt attctgtaaa 300
tactataggg aaagaggctg agcttagaat cttttggttg ttcattgtgt ctgtgctctt 360
atcatcacac tgctcgactt aca 383
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<210> 172
<211> 699
<212> DNA
<213> Homo sapien
<220>
<221> misc_feature
<222> (1)...(699)
<223> n = A,T,C or G
<400> 172
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cggtgcccc tggcacttca gaacctcttc ctctacactt ttggtgcgct tctgaatcta 120
ggtctgcatg ctggcgggcg ctctggccca ggctccttg aaagtttctc aggatgggca 180
gcactcgtgg tgctgagcca ggcactaaat ggactgctca tgtctgctgt catggagcat 240
ggcagcagca tcacacgcct ctttgtggtg tctgctcgc tgggtggtcaa cgcctgctc 300
tcagcagtcc tgctacggct gcagctcaca gccgccttct tcttggccac attgctcatt 360
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ccggaccctg tagattgggc gccaccacca gatccccctc ccaggccttc ctccctctcc 480
catcagcggc cctgtaacaa gtgccttgtg agaaaagctg gagaagttag ggcagccagg 540
ttattctctg gaggttgggtg gatgaagggg tacccttagg agatgtgaag tgtgggtttg 600
gttaaggaaa tgcttaccat cccccaccc caaccaagtt nttccagact aaagaattaa 660
ggtaacatca atacctaggc ctgaggaggc atcaccoga 699
<210> 173
<211> 701
<212> DNA
<213> Homo sapien
<400> 173
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atgtcggaga agaattttg caaaagaaaa atgcctaate agtactaatt taataggatca 120
cattagcagt ggaagaagaa atgttgatat tttatgtcag ctattttata atcaccagag 180
tgcttagctt catgtaagcc atctcgtatt cattagaaat aagaacaatt ttattcgtcg 240
gaaagaactt ttcaatttat agcatcttaa ttgctcagga ttttaaattt tgataaagaa 300
agctccactt ttggcaggag tagggggcag ggagagagga ggctccatcc acaaggacag 360
agacacagg gccagtaggg tagctggttg ctggatcagt cacaacggac tgacttatgc 420
catgagaaga aacaacctcc aaatctcagt tgcttaatac aacacaagct catttcttgc 480
tcacgttaca tgcctatgt agatcaacag cagggtgactc agggacccag gctccatctc 540
catatgagct tccatagtca ccaggacacg ggctctgaaa gtgtcctcca tgcagggaca 600
catgcctctt cttttcattg ggacagagcaa gtcacttatg gccagaagtc acactgcagg 660
gcagtgccat cctgctgtat gcctgaggag gcatcaccga 701
<210> 174
<211> 700
<212> DNA
<213> Homo sapien
<220>
<221> misc_feature
<222> (1)...(700)
<223> n = A,T,C or G
<400> 174
tcgggtgatg cctcctcagg cccctaaatc agagtccagg gtcagagcca caggagacag 60

ggaaagacat	agattttaac	cggccccctt	caggagattc	tgaggctcag	ttcactttgt	120
tgcagtttga	acagaggcag	caaggctagt	ggttaggggc	acggctctct	aagctgeact	180
gcttgatct	gcttccagc	tctgccagga	accagctgcg	tggccttgag	ctgetgacac	240
gcagaaagcc	ccctgtggac	cfagctctct	cgtctgtaag	atgaggacag	gactctagga	300
accctttccc	ttggtttggc	cfcactttca	caggctccca	tcttgaactc	tatctactct	360
tttctgaaa	ccttgtaaaa	gaaaaaagt	ctagcctggg	caacatggca	aaacctgtc	420
tctacaaaa	atacaaaaat	tagttgggtg	tggtggcatg	tgctgttagt	cccagccact	480
tgggaggtgc	tgaggtggga	ggatcacttg	agccccggag	gtggaggttg	cagtgageca	540
agatcatgcc	actgcactcc	agcctgagta	atagagtaag	actctgtctc	aaaaacaaca	600
acaacaacag	tgagtgtgcc	tctgtttccg	ggttggatgg	ggcaccacat	ttatgcatct	660
ctcagatttg	gacgtgcag	cctgaggagg	catcacccga			700

<210> 175
 <211> 484
 <212> DNA
 <213> Homo sapien
 <220>
 <221> misc_feature
 <222> (1) (484)
 <223> n = A,T,C or G
 <400> 175

tatagggcga	attggggccg	agttgcatgn	ccccggccgc	catggccgcg	ggattcgggt	60
gatgcctcct	caggcttgtc	tgccacaagc	tacttctctg	agctcagaaa	gtgccccttg	120
atgagggaaa	atgtcctact	gcactgcgaa	tttctcagtt	ccattttacc	tcccagtcct	180
ccttctaaac	cagttaataa	attcattcca	caagtattta	ctgattacct	gcttgtgcca	240
gggactattc	tcaggctgaa	gaaggtggga	ggggagggcg	gaacctgagg	agqcaoctga	300
gccagcttta	tatttcaacc	atggctggcc	catctgagag	catctcccca	ctctcgccaa	360
cctatcgggg	catagcccag	ggatgcccc	aggcgcccca	ggtagatgc	gtccctttgg	420
cttgctcagt	atgacataca	ccttagctgc	ttagctgggt	ctggcctgag	gaggcatcac	480
ccga						484

<210> 176
 <211> 432
 <212> DNA
 <213> Homo sapien
 <400> 176

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gacaaatgcc	aggtagcgga	attggtactg	gtccaggagt	tatccaggat	agattttcac	180
ccaccatggg	acgtcatcgt	tcaaatcaac	tcttcaatgg	ccatggggga	cacatcatgc	240
ctccacaca	atcgagttt	ggagagatgg	gaggcaagtt	tatgaaaagc	caggggctaa	300
gccagctcta	ccataaccag	agtcaaggac	tcttatccca	gctgcaagga	cagtcgaagg	360
atatgccacc	tgggttttct	aagaaaggac	agcttaatgc	agatgagatt	agcctgagga	420
ggcatcaccc	ga					432

<210> 177
 <211> 788
 <212> DNA
 <213> Homo sapien

<400> 177

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catgctggag	ccaagtgcta	acatgccttg	gttcaaggga	tggaaagtca	cccgttaagga	120
tggcaatgcc	agtgaacca	cgctgcttga	ggctctggac	tgcacacctac	caccaactcg	180
cccaactgac	aagcccttgc	gcctgcctct	ccaggatgtc	tacaaaattg	gtgggtattgg	240
tactgttcc	gttggccgag	tggagactgg	tgttctcaaa	cccggtatgg	tggtaacctt	300
tgctccagtc	aacgttacaa	cggaagtaaa	atctgtcgaa	atgcaccatg	aagctttgag	360
tgaagctctt	cctggggaca	atgtgggctt	caatgtcaag	aatgtgtctg	tcaaggatgt	420
tgcctgtggc	aacgttgctg	gtgacagcaa	aaatgaccca	ccaatggaag	cagctggctt	480
cactgctcag	gtgattatcc	tgaacctatc	aggccaaata	agtgcgggt	atgccctgt	540
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tgcgcgttct	ggtaaaaagc	tggaagatgg	ccctaaattc	ttgaagtctg	gtgatgctgc	660
cattgttgat	atggttcctg	gcaagcccat	gtgtgttgag	agcttctcag	actatccacc	720
tttgggtcgc	tttgcgttgc	gtgatatgag	acagacagtt	gcggtgggtg	tctgggctca	780
acatgcta						788

<210> 178

<211> 786

<212> DNA

<213> Homo sapien

<400> 178

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cacttgggct	gcactttgaa	tgacacactt	ggctttatta	gattcactag	tttttaaaaa	120
attgttgctt	gtttcttttc	attaaaggtt	taatcagaca	gatcagacag	cataattttg	180
tatttaatga	cagnaacgtt	ggtacatttc	ttcatgaatg	agcttgcatt	ctgaagcaag	240
agcctacaaa	aggcacttgt	tataaatgaa	agttctggct	ctagaggcca	gtactctgga	300
gtttcagagc	agccagtgat	tgttccagtc	agtgtgcct	agttatatag	aggaggagta	360
cactgtgcac	tcttctaggt	gtaagggtat	gcaactttgg	atcttaaaat	tctgtacaca	420
tacacaqttt	atatatatgt	atgtatgtat	gaaacatga	aattagtttg	tcaaatatgt	480
gtgtgttttag	tatttttagct	tagtgcaact	atttccacat	tatttattaa	attgatctaa	540
gacactttct	tgttgacacc	ttgaatatta	atgttcaagg	gtgcaatgtg	tattccttta	600
gattgttaaa	gcttaattac	tatgatttgt	agtaaattaa	cttttaaaat	gtatttgagc	660
ccttctgtag	tgctgtaggg	ctcttacagg	gtgggaaaga	ttttaatttt	ccagttgcta	720
attgaacagt	atggcctcat	tatatatttt	gatttatagg	agtttgtgtc	tgggctcaac	780
atgcta						786

<210> 179

<211> 796

<212> DNA

<213> Homo sapien

<400> 179

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acacccccat	ccgcccttg	tttgagtg	agagtttggc	tttggttctt	tgccttgctt	180
ggagtatact	tctaattcct	gttgcctgc	acaagctgaa	taccgagcta	cccacgccca	240
cccaggccag	gtttccaact	atttattact	ttatgtttct	gttccattgc	tgggtccacag	300
aaataagttt	tcctttggag	gaatgtgatt	ataccctttt	aatttctctc	ttttgctttt	360
ttttaatatc	attggtatgt	gtttggccca	gaggaaactg	aaattcacca	tcatcttgac	420
tggcaatccc	attaccatgc	tttttttaaa	aaacgtaatt	tttcttgctt	tacattggca	480
gagtagccct	tcctggctac	tggcctaatt	tagtcactca	gtttctaggt	ggcatttaggc	540
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aaagggctat	gtcaggtttc	aatgctatct	gcttctgttc	ctgctcactg	ttctggattt	660
tgtccttctt	cacccctagc	accagaattt	ccagctctcc	ctccctacct	tccttgtttt	720
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tgggctcaac	atgcta					796

<210> 180
 <211> 488
 <212> DNA
 <213> Homo sapien
 <400> 180
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 aaaacgacgg ccagtgaatt gtaatacagc tcactatagg gcgaattggg cccgacgtcg 120
 catgctcccg gccgccatgg ccgcggggata gcatgttgag cccagacacc tgcagggtcat 180
 ttggagagat ttttcacgtt accagettga tgggtctttt caggaggaga gacactgagc 240
 actcccaagg tgaggttgaa gatttcctct agatagccgg ataagaagac taggagggat 300
 gcctagaaaa tgattagcat gcaaatttct acctgccatt tcagaactgt gtgtcagccc 360
 acattcagct gcttcttggt aactgaaaag agagagggtat tgagactttt ctgatggcgg 420
 ctctaaccatt gtaacacagt aatctgtgtg tgtgtgggtg tgtgtgtgtg tctggggtca 480
 acatgcta

<210> 181

<211> 317

<212> DNA

<213> Homo sapien

<400> 181

tagcatgttg agccagaca eggcgaagggt aegtgatgag tgggggtgatg gcaccgttga 60
 aaaggaggaa cgtcaccccc catgatattg gggacccaga tgatgaacaa tggctccggg 120
 tcaatgcata tttaatccat gatactgctg atttgaagga cctgaacctg aagtttgtgc 180
 tgcaggttta tggggactat tacctcaccg gtgateaaaa ctctctgaag gacatgttgc 240
 ctgtgtgtct agtaagggtat gcacatgcag tggccagtgt gccaggggta tggttggtgt 300
 ctggggtcaa catgcta 317

<210> 182

<211> 507

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(507)

<223> n = A,T,C or G

<400> 182

tagcatgttg agcccagaca ctggctgtta gccaaatcct ctctcagctg ctccctgtgg 60
 tttggtgact caggattaca gaggcatcct gtttcaggga acaaaaagat tttagctgcc 120
 agcagagagc accacataca tttagaattgt aaggactgct accctccttca agaacaggag 180
 tgagggtggt ggtgaatggg aatggaagcctgcatcct gatgcatttg tgcctcttca 240
 aatcctgtct tagtcttagg aaaggaagta aagtttcaag gacggttccg aactgctttt 300
 tgtgtctggg ctcaacatgc tatcccgccg ccattggcgg cgggagcatg cgacgtcggg 360
 cccaattgcg cctatagtga gtgtattac aattcactgg cgtcgtttt acaacgtcgt 420
 gactgggaaa accctggcgt tacccaactt aatcgccttg cagcacatcc ccdtttccca 480
 gctggcgtaa tancgaaaag gcccgca 507

<210> 183

<211> 227

<212> DNA

<213> Homo sapien

<400> 183

gatttacgct gcaacactgt ggaggtagcc ctggagcaag gcaggcatgg atgcttctgc 60
 aatccccaaa tggagcctgg tatttcagcc aggaatctga gcagagcccc ctctaattgt 120
 agcaatgata agttattctc tttgttcttc aaccttccaa tagccttgag cttccagggg 180
 agtgtcgta atcattacag cctgggtctc acagtgttgc agcgtaa 227

<210> 184

<211> 225

<212> DNA

<213> Homo sapien

<400> 184

ttacgctgca acactgtgga gcagattaac atcagacttt tctatcaaca tgactggggg 60
 tactaaaaag acaacaaatc aatggcttca aaagtctaag gaataatttc gatacttcaa 120
 ctttataaaa cctgacaaaa ctatcaatca agcataaaga cagatgaaga acatttccag 180
 attttggcca atcagatatt ttacctccac agtgttgcag cgtaa 225

<210> 185

<211> 597

<212> DNA

<213> Homo sapien

<400> 185

ggcccgacgt cgcattgctc cggccgcat ggcccgggga ttcgttaggg tctctatcca 60
 ctgggaccca taggctagtc agagtattta gagttgagtt cctttctgct tcccagaatt 120
 tgaaagaaaa ggagttaggt gatagagctg agagatcaga tttgcctctg aagcctgttc 180
 aagatgtatg tgctcagacc ccaccactgg ggctgtggg tgaggtcctg ggcattctatt 240
 tgaatgaatt gctgaagggg agcactatgc caaggaaggg gaacccatcc tggcattggc 300
 acaggggtca ccttatccag tgctcagtc ttctttgctg ctacctggtt ttctctcata 360
 tgtgaggggc aggtaagaag aagtgcccg tggttggtgca gttttagaac atctaccagt 420
 aagtggggaa gtttccaaaa gcagcagctt tggtttgtgt attttcacct tcagttagaa 480
 gaggaaggct gtgagatgaa tgtagttga gtggaaaaga cgggtaagct tagtggtatg 540
 agaccctaac gaatcactag tgccgcgcgc ttgcaggtcg accatatggg agagctc 597

<210> 186

<211> 597

<212> DNA

<213> Homo sapien

<400> 186

ggcccgaaat tgcattgttc cggccgcat ggcccgggga ttcgttaggg tctctatcca 60
 ctacctaaaa aatccccaac atataactga actcctcaca cccaattgga ccaatccatc 120
 accccagagg cctacagatc ctctttgat acataagaaa atttcccaa actacctaac 180
 tatatcattt tgcaagattt gttttaccaa attttgatgg cctttctgag cttgtcagtg 240
 tgaaccacta ttacgaacga tcggatatta actgcccctc accgtccagg tgtagctggc 300
 aacatcaagt gcagtaaata ttcattaagt tttcacctac taaggtgctt aaacacccta 360
 gggtgccatg tcggtagcag atcttttgat ttgtttttat ttccataag ggtcctgttc 420
 aaggtcaatc atacatgtag tgtgagcagc tagtcactat cgcattgact ggagggtagt 480
 aatagaggcc tcctttgctg ttaaagaact cttgtcccag cctgtcaaag tggatagaga 540
 ccctaacgaa tcactagtgc ggccgcctgc aggtcgacca tatgggagag etcccaa 597

<210> 187

<211> 324

<212> DNA

<213> Homo sapien

<400> 187

```
tctttagggg ctctatccac ttgcaggtaa aatccaatcc tgtgtatata ttatagtctt 60
ccatatgtag tggttcaaga gactgcagtt ccagaaagac tagccgagcc catccatgtc 120
ttccacttaa cctgcttttg ggttacacat ctttaacttt ctgttcaagt ttctctgtgt 180
agtttatagc atgagtattg ggawaatgcc ctgaaacctg acatgagatc tgggaaacac 240
aaacttactc aataagaatt tctcccatat ttttatgatg gaaaaatttc acatgeacag 300
aggagtggat agagacccta acga 324
```

<210> 188

<211> 178

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(178)

<223> n = A,T,C or G

<400> 188

```
gcgcgggggat tgggggtgat acctctcat gccaaaatac aacgtntaat ttcaacaactt 60
gccttccaat ttacgcattt tcaatttgcg ctccccattt gttgagtcac aacaaacacc 120
attgcccgaga aacatgtatt acctaacatg cacataactct taaaactact catccctt 178
```

<210> 189

<211> 367

<212> DNA

<213> Homo sapien

<400> 189

```
tgacaccttg tccagcatct gacacagctc tgggtotttg aaaatattgg ataatgaaa 60
atgaatttct ttagcaagtg gtataagctg agaataacg tatcacatat ccttattcta 120
agacacattc agtgtccctg aaattagaat aggacttaca ataagtgtgt tcaactttctc 180
aatagctgtt attcaattga tggtaggcct taaaagtcaa agaaatgaga gggcatgtga 240
aaaaaagctc aacatcactg atcattagaa aacttccatt caaaccccca atgagatacc 300
atctcatacc agtcagaatg gctattatta aaaagtcaaa aaataacaga tgcctggacaa 360
gggtgtca 367
```

<210> 190

<211> 369

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(369)

<223> n = A,T,C or G

<400> 190

```
gacaccttgt ccagatctg acaacgctaa cagcctgagg agatctttat ttattttatt 60
agtttttact ctggctaggc agatgggtgc taaaacattc atttaccat ttattcattt 120
aattgttctt gcaaggcta tggatagagt attgtccagc actgctctgg aagctaggag 180
catggggatg aacaagatag gctacatcct gttccacag aacttccact ttagtctggg 240
aaacagatga tatatacaaa tatataaatg aattcaggta gttttaagta cgaaaagaat 300
```

aagaaagcag agtcatgatt tanaatgctg gaaacagggg ctattgcttg agatattgaa 360
 ggtgcccaa 369

<210> 191

<211> 369

<212> DNA

<213> Homo sapien

<400> 191

tgacaccttg tccagcatct gcacagggaa aagaaactat taccagagt aacaggcaac 60
 ctacagaatg ggagaaaatt ttgcaatct atccatctga caaagggtta atatccagaa 120
 tctacaaaga acttatacaa atttacaaga aacaaacaaa caaacaactc ctcaaaaagt 180
 ggggtgaagg tgtgaacaga cacttctcaa aagaagacat ttatggggcc acaaaacata 240
 tgaaaaaag ctcatcatca ctggctacta gataaatgca aatcaaaacc acaatgagat 300
 accatctcat tccagttaga atggcaatca taaaaaagtc aggaacaac agatgctgga 360
 caaggtgtc 369

<210> 192

<211> 449

<212> DNA

<213> Homo sapien

<400> 192

tgacgcttgg ccacttgaca ctccatcttt gcacagaaaa acttctttac agatttaatt 60
 caagactggg ctagtgcag tcctccagac attttttcat ttgttcata tacgtggaat 120
 tttaaaatca tgtttcatca gtttgaaatg atttgggctg ctaatcaaca caattggatc 180
 gactgttcta ctaacaaca ggaaaatgtg tatctggcag cctgtggaga aacactaac 240
 attgattttt ctttgccttt tacggacttt gtccagctta catgtaatac caagtctct 300
 ttaagaggag aagatgttga tcttcatttg tttctaccag actgccacc tagtaaatat 360
 tctttattta tgctggtaaa aaattgccat ccaaataaga tgattcatga tactggtatt 420
 cctgctgagt gtcaagtggc caagcgta 449

<210> 193

<211> 372

<212> DNA

<213> Homo sapien

<400> 193

tgacgcttgg ccacttgaca ccagggatgt akcagttgaa tataatcctg caattgtaca 60
 tattggcaat ttcccatcaa acattctaga aagagacaac caggattgct aggcataaa 120
 agctgcaata aataactggt aattgcagta atcatttcag gccaatcaa tccagtttgg 180
 ctacagagggt cctttggctg agagaagagg tgagatataa tgtgttttct tgcaacttct 240
 tggaagaata actccacaat agtctgagga ctagatacaa acctatttgc cattaaagca 300
 ccagagtctg ttaattccag tactgataag tgttgagat tagactccag tgtgtcaagt 360
 ggccaagcgt ca 372

<210> 194

<211> 309

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1) ... (309)

<223> n = A, T, C or G

<400> 194
 tgacgcttgg ccacttgaca cttatgtaga atccatcgtg ggctgatgca agccctttat 60
 ttaggcttag tgttgtgggc accttcaata tcacactaga gacaaacgcc acaagatctg 120
 cagaaacatt cagttctgan cactcgaatg gcaggataac tttttgtgtt gtaatccttc 180
 acatatacaa aaacaaactc tgcantctca cgttacaaaa aaacgtactg ctgtaaaata 240
 ttaagaaggg gtaaaggata ccatctataa caaagtaact tacaactagt gtcaagtggc 300
 caagcgtca 309

<210> 195

<211> 312

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(312)

<223> n = A,T,C or G

<400> 195
 tgacgcttgg ccacttgaca cccaatctcg cacttcatcc tcccagcacc tgatgaagta 60
 ggactgaac tatccccact tcccagatga ggggaccaan gtacacatta ggaccoggat 120
 gggagcacag atttgtccga tcccagactc caagcactca gcgtcactcc aggacagcgg 180
 ctttcagata aggtcacaaa catgaatggc tcogacaacc ggagtcagtc cgtgotgagt 240
 taaggcaatg gtgacacgga tgcacgtgtn acctgtaatg gttcatcgta agtgtcaagt 300
 ggccaagcgt ca 312

<210> 196

<211> 288

<212> DNA

<213> Homo sapien

<400> 196
 tgtatcgacg tagtgggtctc ctcagccatg cagaactgtg actcaattaa acctctttcc 60
 tttatgaatt acccaatctc gggtagtgte tttatagtag tgtgagaatg gactaataca 120
 agtacatttt acttagtaat aataataaac aaatatatta cattttttgtg tatttactac 180
 accatatttt ttattgttat tgtagtgtac accttctact tattaaaaga aataggcccc 240
 aggcgggcag atcacgaggt caggagatgg agaccactac gtcgatac 288

<210> 197

<211> 289

<212> DNA

<213> Homo sapien

<400> 197
 ttgggcacct tcaatatcat gacaggtgat gtgataacca agaaggctac taagtgatta 60
 atgggtgggt aatgtatata gagtaggtac actggacaga ggggtaattc atagccaagg 120
 caggagaagc agaatggcaa aacatttcat cacactactc aggatagcat gcagtttaaa 180
 acctataagt agtttatttt tggaaatttc cacttaatat tttcagactg caggtaacta 240
 aactgtggaa cacaagaaca tagataaggg gagaccacta cgtcgatac 289

<210> 198

<211> 288

<212> DNA

<213> Homo sapien

<400> 198
 gtatcgacgt agtgggtctcc caagcagtgga gaagaaaacg tgaaccaatt aaaatgtatc 60
 agatacccca aagaaaggcg cttgagtaaa gattccaagt gggtcacaat ctcagatctt 120
 aaaattcagg ctgtcaaaga gatttgctat gaggttgctc tcaatgactt caggeacagt 180
 cggcaggaga ttgaagccct ggccattgtc aagatgaagg agctttgtgc catgtatggc 240
 aagaaagacc ccaatgagcg ggactcctgg agaccactac gtcgatac 288

<210> 199

<211> 1027

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1) ... (1027)

<223> n = A,T,C,G

<400> 199
 gcttttttggg aaaaacncaa ntgggggaaa gggggnntnn tngcaagggg ataaaggggg 60
 aaaaaagggg tttcccccatt caggagagtg taaaaagncg gccaggggat tgtaaanagga 120
 ttcaataata gggggaatgg gccnngaagt tgaaggttc cngcccgcca tgncccgagg 180
 atttagtgac attacgacgs tgtaataaaa gtgggsccaa waaatatttg tgatgtgatt 240
 tttgaccag tgaaccatt gwacaggacc tcatttccty tgagatgrta gccataatca 300
 gataaaagrt tagaagtytt tctgcacgtt aacagcatca ttaaattggag tggcatcacc 360
 aatttcaccc tttgttagcc gataccttcc ccttgaaggc attcaattaa gtgaccaatc 420
 gtcatacgag aggggatggc atggggattg atgatgatat caggggtgat accttcacag 480
 gtgaaaggca taccctcttg tctatactga ataccacaag tacccttttg accatgtcga 540
 ctacaaaatt tgtctccaat ctgtgtwatc cctaacagag cgtaccetta ttttacaana 600
 tttatatcct tcttgattga gagttaccat aacctgatcc acaatgcccg tctcgtwtgt 660
 tctgagaaaa gtgtacagt ctctcttggt atagcgtcta ttggtgctct ccaattcacc 720
 tttcatttttc aggaagggtg aactgttttg ctataataa cmtcatctcc tgatacmcga 780
 aacccckgga rctatcaaac catatcatc cgggttctt watgtymcta aatccctatt 840
 ggggcccct gcagggtcaac atatnggaaa accccccacc ccttnggagc ntaccttgaa 900
 ttttccatat gtccntaaa ttanctngnc ttanctggc cntaacctnt tccggtttaa 960
 attgtttccg ccccnttcc cnccttnna accggaaacc ttaattttna accnggggtt 1020
 cctatcc 1027

<210> 200

<211> 207

<212> DNA

<213> Homo sapien

<400> 200
 agtgacatta cgacgtggc catcttgaat cctagggcat gaagttggcc caaagttcag 60
 cacttggtta agcctgatcc ctctggttta tcacaaagaa taggatggga taaagaaagt 120
 ggacacttaa ataagctata aatttatatg tcttgtcta gcaggagaca actgcacagg 180
 tatactacca ggcgtgtaat gtcacta 207

<210> 201

<211> 209

<212> DNA

<213> Homo sapien

<400> 201

tgggcacctt caatatctat taaaagcaca aatactgaag aacacaccaa gactatcaat 60
 gaggttacat ctggagtctt cgatatatca ggaaaaaatg aagtgaacat tcaacagagtt 120
 ttacttcttt gggaactcaa atgctagaaa agaaaagggt gccctctttc tctgggttcc 180
 tggctctatt cagcgtcgta atgtcacta 209

<210> 202
 <211> 349
 <212> DNA
 <213> Homo sapien
 <220>
 <221> misc_feature
 <222> (1) ... (349)
 <223> n = A,T,C or G

<400> 202

ntacgctgca aactgtgga gccactgggt tttattcccg gcaggttatc cagcaaacag 60
 tcaactgaaca caccgaagac cgtgggtatg taaccgttca cagtaatcgt tccagtcgtc 120
 tgcgggaccc cgacgagcgt cactgggtac agaccagatt cagccggaag agaaagcggc 180
 gcaggagag actcgaactc cactcgcgtg gtgagcagcc ccattgtttc aactcgaagt 240
 tcaaacggca ttgggttata taccatcagc tgaacttca acacatctcc ttgaaccgac 300
 tggaaatcta tttcttgggt ccgtctttct ccacagtgtt gcagcgca 349

<210> 203
 <211> 241
 <212> DNA
 <213> Homo sapien

<400> 203

tgctctcttt gccttaccaa cccaaagccc actgtgaaat atgaagtgaat gacaaaatt 60
 cagttttcaa cgcaatatag tatagtttat tctgattctt tgcattccag gacactttaa 120
 acaactgcta ccaccaccac caacctaggg tatbtaggatt ctccacagac cagaaattat 180
 ttctcttttg agtttcaggc tcctctggga ctctctgttca tcaatgggtg gtaaatggct 240

<210> 204
 <211> 248
 <212> DNA
 <213> Homo sapien

<400> 204

tagccattta ccccatct gcaaaccswg acmwwcargr cywgwackya ggcgatttga 60
 agtactggta atgctctgat catgttagtt acataagtgt ggtcagtta caaaaattca 120
 cagaactaaa tactcaatgc tatgtgttca tgtctgtgtt tatgtgtgtg taatgtttca 180
 attaatgttt ttttaaaaaa agagatgatt tccaaataag aaagccgtgt tggtaaggca 240
 agaggago 248

<210> 205
 <211> 505
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1) ... (505)

<223> n = A, T, C or G

<400> 205

```
tacgctgcaa cactgtggag ccattcatac aggtccctaa ttaaggaaca agtgattatg 60
ctacctttgc acggttaggg taccgcggcc gttaaactatg tgcactggg caggcgggtgc 120
ctctaatact ggtgatgcta gaggtgatgt ttttggtaaa caggcggggc aagatttgcc 180
gagttccttt tacttttttt aacctttcct tatgagcatg cctgtgttgg gtgacagtg 240
ggggtataaa tgacttggtg gttgattgta gatattgggc tgttaattgt cagttcagtg 300
ttttaatctg acgcaggctt atgcggagga gaatgttttc atgttactta tactaacatt 360
agttcttcta tagggtgata gattggtcca attgggtgtg aggagtccag ttatatgttt 420
gggatttttt aggtagtggg tgttgancct gaacgctttc ttaattggtg gctgctttta 480
rgcctactat ggggtgtaaa tggct 505
```

<210> 206

<211> 179

<212> DNA

<213> Homo sapien

<400> 206

```
tagactgact catgtccctt accaaagccc atgtaaggag ctgagttctt aaagactgaa 60
gacagactat tctctggaga aaaataaaat ggaaattgta ctttaaaaaa aaaaaaatc 120
ggcgggcat ggtagcacac acctgtaatc ccagctacta ggggacatga gtcagtcta 179
```

<210> 207

<211> 176

<212> DNA

<213> Homo sapien

<400> 207

```
tagactgactc atgtccccta cccaccttc atgctgtgctg ccgtgttctt accaggtcac 60
tagactggtac tggtcagtgg cctgggggtt ggggacctct attatatggg atacaaattt 120
aggagtggga attgacacga tttagtact gatgggatat ggggtgtaaa tggcta 176
```

<210> 208

<211> 196

<212> DNA

<213> Homo sapien

<400> 208

```
agactgactc atgtccccta tttacaggg tctctagtgc tgtgaaaaaa aaaaatgctg 60
aacattgcat ataacttata ttgtaagasa tactgtacaa tgactttatt gcatctgggt 120
agctgtaagg catgaaggat gccagaagt ttaaggaata tgggtggtaa atggctaggg 180
gacatgagtc agtcta 196
```

<210> 209

<211> 345

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1) ... (345)

<223> n = A, T, C or G

<400> 209

gacgcttggc cacttgacac cttttatattt ttaaggattc ttaagtcatt tangtnactt 60
 tgtaagtttt tctgtgccc ccataagaat gatagcttta aaaattatgc tggggtagca 120
 aagaagatac ttctagcttt agaatgtgta ggtatagcca ggattcttgt gaggaggggt 180
 gatttagagc aaattttctta ttctccttgc ctcattctgta acatggggat aataatagaa 240
 ctggcctgac aaggttggaa tttagtattac atggtaataa catgtaaaat gtttagaatg 300
 gtgccaagta tctagggaag acttgggcat ggggtgtaaa tggct 345

<210> 210
 <211> 178
 <212> DNA
 <213> Homo sapien

<400> 210
 gacgcttggc cacttgacac tagagtaggg tttggccaac tttttctata aaggaccaga 60
 gagtaaatat ttcaggcttt gtgggttgtg cagtctctct tgcaactact cagctctgcc 120
 attgtagcat agaaatcagc catagacagg acagaaatga atgggtggtg aatggcta 178

<210> 211
 <211> 454
 <212> DNA
 <213> Homo sapien

<400> 211
 tgggcacctt caatatctat ccagcgcac taaattcgct tttttcttga ttaaaaattt 60
 caccacttgc tgtttttgct catgtatacc aagtagcagt ggtgtgagc catgcttgtt 120
 ttttgattcg atatcagcac cgtataagag cagtgtttg gccattaatt tatcttcatt 180
 gtagacagca tagttagag tggatctcc atactcatct ggaatatttg gatcagtgcc 240
 atgttccagc aacattaacg cacattcatc ttcttggcat tgtacggcct ttgtcagagc 300
 tgtctctttt ttgttgtcaa ggacattaag ttgacatcgt ctgtccagca cagattttac 360
 tacttctgaa ttccatttg cagaggccag atgtagagca gtctcttttt gettgctcct 420
 cttgttcaca tcaagtgtcc tgagcataac ggaa 454

<210> 212
 <211> 337
 <212> DNA
 <213> Homo sapien

<400> 212
 tccgttatgc caccagaaa acctactgga gttacttatt aacatcaagg ctggaaccta 60
 tttgcctcag tcttatctga ttcatgagca catggttatt actgatcgca ttgaaaacat 120
 tgatcacctg ggtttcttta tttatcgact gtgtcatgac aaggaaactt acaaactgca 180
 acgcagagaa actattaaag gtattcagaa acgtgaagcc agcaattggt tcgcaattcg 240
 gcattttgaa aacaaatttg cgtggaaac tttatttgt tcttgaaacag tcaagaaaaa 300
 cattattgag gaaaattaat atcacagcat aacggaa 337

<210> 213
 <211> 715
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc feature
 <222> (1) . . (715)
 <223> n = A,T,C or G

<400> 213

```

tcgggtgatg cctcctcagg catcttccat ccatctcttc aagattagct gtcccaaatg      60
tttttccttc ttttctttac tgataaattt ggactccttc ttgacactga tgacagcttt      120
agtatccttc ttgtcacctt gcagacttta aacataaaaa tactcattgg ttttaaagg      180
aaaaaagtat acattagcac tattaagctt ggccttgaaa cattttctat cttttattaa      240
atgtcggtta gctgaacaga attcatttta caatgcagag tgagaaaaga agggagctat      300
atgcatttga gaatgcaagc attgtcaaat aaacatttta aatgctttct taaagtgagc      360
acatacagaa atacattaag atattagaaa gtgtttttgc ttgtgtacta ctaattaggg      420
aagcaccttg tatagtccct cttctaaaat tgaagtagat tttaaaacc catgtaattt      480
aattgagctc tcagttcaga ttttaggaga attttaacag ggatttggtt ttgtctaaat      540
ttttgtcaatt tntttagtta atctgtataa ttttataaat gtcaaactgt atttagtccg      600
ttttcatgct gctatgaaag aaataccan gacagggtta tttataaang gaaagangtt      660
aatttgactc ccagttcaca ggctgagga ngnatcnccc gaaatcctta ttgag      715

```

<210> 214

<211> 345

<212> DNA

<213> Homo sapien

<220>

```

<221> misc_feature
<222> (1)..(345)
<223> n = A,T,C,G
<400> 214
ggtaangngc atacntcggg gtcctggcgg ccggagtcgg gggattcggg tgatgcctcc      60
tcaggcccac ttgggcctgc ttttcccaa tggcagctcc tctggacatg ccattccttc      120
tcccacctgc ctgattcttc atatgttggg tgcctctgtt tttctgggtc tatttcctga      180
ctgctgttca gctgccactg tctgtcaaag cctgcctttt taaatgcctc accattcctt      240
catttgtttc ttaaataatg gaagtgaag tgccacctga ggccgggcac agtgggtcac      300
gcctgtaatc ccagcacttt gggagcctga ggaggcatca cccga      345

```

<210> 215

<211> 429

<212> DNA

<213> Homo sapien

<400> 215

```

ggatgatgct cctcaggcga agctcaggga ggacagaaac ctcccggtga gcagaagggc      60
aaaagctcgc ttgatcttga ttttcagtac gaatacagac cgtgaaagcg gggcctcacg      120
atccttctga ccttttgggt ttttaagcagg aggtgtcaga aaagttacca cagggataac      180
tggtctgtgg cggccaagcg ttcatagcga cgtcgctttt tgatccttcg atgtcggctc      240
ttctatcat tgtgaagcag aattcaccaa gcgttgatt gttcacccac taatagggaa      300
cgtgagctgg gtttagaccg tcttgagaca ggtagtttt accctactga tgatgtgtkg      360
ttgccatggt aatcctgctc agtacgagag gaaccgcagg ttcasacatt tgggtgtatgt      420
gcttgctt      429

```

<210> 216

<211> 593

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)..(593)

<223> n = A,T,C or G

<400> 216

```
tgacacctat gtcnccatc tgttcacagt ttccacaaat agccagcctt tggccacctc 60
tctgtcctga ggtatacaag tatatcagga ggtgtatacc ttctcttctc tccccacca 120
aagagaacat gcaggtcttg gaagctgtct taggagcctt tgggctcaga atttcagagt 180
cttgggtacc ttggatgttg tctggaagga gaaacattgg tcttgataaa ggagtacagc 240
cggaggaggg tcacagagcc ctccagctcaa gcccctgtgc tcttagtctaa aagcagcttt 300
ggatgaggaa gcaggttaag taacatacgt aagcgtacac aggtagaagc tgetgggagt 360
cagaattgca cagtgtgtag gagtagtacc tcaatcaatg agggcacaatc aactgaaaga 420
agaagacoma ttaatgaatt gcttangggg aaggtatcaag gctatcatgg agatctttct 480
aggaagatta ttgtttanaa ttatgaaagg antagggcag ggacagggcc agaagtanaa 540
ganaacattg cctatanccc ttgtcttgca cccagatgct ggacaagggt tca 593
```

<210> 217

<211> 335

<212> DNA

<213> Homo sapien

<400> 217

```
tgacaccttg tccagcatct gacgtgaaga tgagcagctc agaggagggtg tcttggaattt 60
cctggttctg tgggctccgt ggcaatgaat tcttctgtga agtggatgaa gactacatcc 120
aggacaaatt taatcttact ggactcaatg agcaggctcc tcaactatga caagctctag 180
acatgatctt ggacctggag cctgatgaag aactggaaga caaccccaac cagagtgacc 240
tgattgagca ggcagccgag atgctttatg gattgatcca cgcccgctac atctctacca 300
accgtggcat cgccagatg ctggacaagg tgtca 335
```

<210> 218

<211> 248

<212> DNA

<213> Homo sapien

<400> 218

```
tacgtactgg tcttgaaggc cttaggtaga gaaaaaatgt gaatatttaa tcaaagacta 60
tgtatgaaat gggactgtaa gtacagaggg aagggtggcc cttatcgcca gaagttggta 120
gatgagtcac cgtcatgaaa tggtgtgtca ctgcccagaca tttgcgaat tactgaaatt 180
cctgataatt agtgcgaatt ctaacgttgt tcatctaaga ttatggttcc atgtttctag 240
tactttta 248
```

<210> 219

<211> 530

<212> DNA

<213> Homo sapien

<220> misc_feature

<222> (1)...(530)

<223> n = A,T,C or G

<400> 219

```
tgacgcttgg ccacttgaca caagtagggg ataaggacaa agacccatna ggtggcctgt 60
cagccttttg ttactgttgc ttccctgtca ccacggcccc ctctgtaggg gtgtgctgtg 120
ctctgtggac attggtgcat ttccacacat accattctct ttctgcttca cagcagtcct 180
gaggcgggag cacacaggac taccttgtca gatgangata atgatgtctg gccaaetcac 240
cccccaacct tctcactagt tatangaaga gccangccta naacctteta tcttgncccc 300
```

```

ttgccctatg acctcatccc tgttccatgc cctattctga tttctggtga actttggagc 360
agcctggttt ntccctctca ctccagctc tctccatacc atggtanggg ggtgctgttc 420
cacncaaang gtcagggtgtg tctggggaat cctnananct gccnggagtt tccnangcat 480
tcttaaaaac cttcttgctt aatcanatng tgtccagtgg ccaaccntcn 530

```

<210> 220

<211> 531

<212> DNA

<213> Homo sapien

<400> 220:

```

tgacgcttgg ccacttgaca ctaaataagca tcttctaaag gcctgattca gagggtgtgga 60
aaattctccc aytgtcaggg atgtgcagga acagggctgc tctgtgtctc actttacctg 120
ctgtgtttct gctggaaag gagggaagag gaatggctga tttttacctt atgtctccca 180
gtttttcata ttcttcttgg atcctcttct ctgacaactg ttcccttttg gtcttcttct 240
tcttgctcag a agcaggtc tctttaaaac tgagaaggga gaatgagcaa atgattaaag 300
aaaacacact tctyagggcc agagatcaaa tattaggtaa atactaaacc gcttgctgc 360
tgtggctact ttctctctct ttccatgct ctatccctct atccccacc tattcatatg 420
gcttttatct gccaggttat ccggcctctc atcaaccttc tcccctagcc tactggggga 480
tatccatctg ggtctgtctc tgggtgtattg gtgtcaagtg gccaaagcgtc a 531

```

<210> 221

<211> 530

<212> DNA

<213> Homo sapien

<400> 221

```

attgacgctt ggccacttga caccgcctg cctgcaatac tggggcaagg gccttcactg 60
ctttctgcc accagctgcc actgcacaca gagatcagaa atgctaccaa ccaagactgt 120
tggtctcag cctctctgag gagaaagagc agaagcctgg aagtcagaag agaagctaga 180
tcggtacgg ccttggcagc cagcttcccc acctgtggca ataaagctgt gcatggctta 240
acaatggggg caccctctga gaaacacatt gttaggcaat tcggcgtgtg ttcatcagag 300
catatttaca caaacctcga tagtgagcc tactatccac tattgctcct acgtgcaaa 360
cctgaacagc atgggactgt actgaatact ggaagcagct ggtgatggtt cttatttgtg 420
tatctaaaca cagagaaggt acagtaagaa tatggtaaca taaacttaca gggaccgcca 480
tcttatatgc agtctgtgtg yaccaaaatg tgtcaagtgg ccaagcgtca 530

```

<210> 222

<211> 578

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(578)

<223> n = A, T, C or G

<400> 222

```

tgtatcgacg tagtggctct cgggctacta ggccgttgtg tggtggtagt acctgggtca 60
ctgaaaggcg catctcctc cccgcgtcgc cctgaagcag ggggaggact tcgccagcc 120
aaggcagttg tatgagtttt agctgcggca cttegagacc tctgagccca cctccttcag 180
gagccttccc cgattaaagga agccagggtt aggattcctt cctccccag acaccacgaa 240
caaaccacca cccccctat tctggcagcc catatacatc agaacgaaac aaaaataaca 300
aataaacnaa aacaaaaaaa aaaagagaag gggaaatgta tatgtctgtc catcctgttg 360
cttagcctg tcagctccta nagggcaggg accgtgtctt ccgaatggtc tgtgcagcgc 420

```


cgactgcggg aagtatcgga ggaggaagca gagtcagcag aagtgaacg gtgggcccgg 480
 cggctcttgg gggctggtgt tgtacttcga gaccgcttcc gcttttctc tttagatttac 540
 gtttgccttt tggagtggga naccactacn tcnataca 578

<210> 223
 <211> 578
 <212> DNA
 <213> Homo sapien

<400> 223

tgtatcgacg tagtgggtctc ctcttgcaaa ggactggctg gtgaatgggt tccctgaatt 60
 atggacttac cctaaacata tottatcatc attaccagtt gcaaaatatt agaattgtgt 120
 gtcactgttt catttgattc ctagaagggt agtcttagat atgttacttt aacctgtatg 180
 ctgtagtgtc ttgaatgcat tttttgtttg catttttgtt tgoccaacct gtcatttata 240
 gctgcttagg tctggactgt cctggataaa gctgttaaaa tattcaccag tccagccatc 300
 ttacaagcta attaatgaa ctaaatgctt ccttgttttg ccagacttgt tatgtcaatc 360
 ctcaatttct ggggtcattt tgggtgcctt aaatcttagg gtgtgacttt cttagcatcc 420
 tgtaacatcc attcccaagc aagacaaact tcacataata ctttcagaa gttcattgct 480
 gaagccttcc cttcaccacg cggagcaact tgattttcta caacttccct catcagagcc 540
 acaagagtat gggatatgga gaccactacg tcgataca 578

<210> 224
 <211> 345
 <212> DNA
 <213> Homo sapien

<220>

<221> misc_feature

<222> (1) 77(345)

<223> n = A,T,C or G

<400> 224

tgtatcgacg tantgggtctc ccaagggtgt gggatttcag gcatgagcca ccactcccag 60
 gtggatcttt ttctttatac ttacttcatt aggtttctgt tattcaagaa gtgtagtggg 120
 aaaagtcttt tcaatctaca tggttaaata atgatagcct gggaaataaa tagaaatttt 180
 ttctttcatc tttaggttga ataaagaac agaaaaata gaacatactg aaaataatct 240
 aagttccaac catagaagaa ctgcagaaga aatgaagaaa gtgatgatga ttttagattt 300
 gatattgatt tagaagacac aggaggagac cactacgtcg ataca 345

<210> 225
 <211> 347
 <212> DNA
 <213> Homo sapien

<400> 225

tgtatcgacg tagtgggtctc caaactgagg tatgtgtgcc actagcacac aaagccttcc 60
 aacagggacg caggcacagg cagtttaaa ggaatctgtt tctaaattaa ttccacctt 120
 ctctaagtat tctttcttaa aactgatcaa ggtgtgaagc ctgtgtcttt tcccaactcc 180
 cctttgacaa cagccttcaa ctaacacaag aaaaggcatg tctgacactc ttctgagtc 240
 tgactctgat acgttgttct gatgtctaaa gagctccaga acaccaaggg gacaattcag 300
 aatgctgggt tataacagac tccaatggag accactacgt cgataca 347

<210> 226

<211> 281

<212> DNA

<213> Homo sapien
 <220>
 <221> misc_feature
 <222> (1) .. (281)
 <223> n = A,T,C or G
 <400> 225
 aggnngggga ntgtatcgac gtagtggctt cccaacagtc tgtcattcag tctgcaggtg 60
 tcagtgtt t ggacaatgag gcaccattgt cacttattga ctctcagct ctaaattgctg 120
 aaattaaatc ttgtcatgac aagtctggaa ttcctgatga ggttttacaa agtatttttg 180
 atcaatactc caacaaatca gaaagccaga aagaggatcc tttcaatatt gcagaaccac 240
 gagtggattt acacaccta ggagaccact agtcgatac a 281
 <210> 227
 <211> 3646
 <212> DNA
 <213> Homo sapien
 <400> 227
 gggaacact tctccagc cttgtaaggg ttggagcct ctccagtata tgctgcagaa 60
 tttttctctc ggtttctcag aggattatgg agtcgcctt aaaaaaggca agctctggac 120
 actctgcaa gtagaatggo caaagtgttg agttgagtgg ccccttgaag ggtcactgaa 180
 cctcacaatt gttcaagctg tgtggcgggt tgttactgaa actcccgcc tccctgatca 240
 gtttccctac attgatcaat ggctgagttt ggtcaggagc accccttcg tggctccact 300
 catgcaccat tcataatttt acctccaagg tctcctgag ccagaccgtg ttttgcctc 360
 gaccctcagc cggttcggct cgccctgtac tgcctctctc tgaagaagag gagagtctcc 420
 ctacccagc cccaccgct taaaaccagc ctactccctt agggtcaccc catgtctcct 480
 cggtatgtc ccctgtaggc tcatcaccca ttgctcttg gttgcaaccg tgggtggagg 540
 aagtagcccc tctactacca ctgagagagg cacaagtccc tctgggtgat gagtgtcca 600
 ccccttccct ggtttatgtc ccttctttct acttctgact tgtataattg gaaaacccat 660
 aatcctccct tctctgaaa gccccaggct ttgacctcac tgatggagtc tgtactctgg 720
 acacattggc ccacctggga tgaactgtcaa cagctccttt tgaccctttt cacctctgaa 780
 gagagggaaa gtatccaaag agaggccaaa aagtacaacc tcacatcaac caataggcgg 840
 gaggaggaag ctagaggaat agtgattaga gacccaattg ggacctaat gggacccaaa 900
 tttctcaagt ggaggagaa cttttgacga tttccaccgg tatctcctcg tgggtattca 960
 gggagctgct cagaaaccta taaacttgct taaggcgact gaagtcgtcc aggggcatga 1020
 tgagtcacca ggagtgttt tagagcact ccaggaggct tatcagattt acaccccttt 1080
 tgacctggca gccccgaaa atagccatgc tottaatttg gcatttgtgg ctccaggcagc 1140
 cccagatagt aaaaggaaac tccaaaaact agagggattt tgctggaatg aataccagtc 1200
 agctttttaga gatagcctaa aagggttttg acagtcaaga ggttgaaaaa caaaaacaag 1260
 cagctcaggc agctgaaaaa agcoactgat aaagcatcct ggagtatcag agtttactgt 1320
 tagatcagcc tcatgtgact tcccctccca catggtgttt aaatccagct acactacttc 1380
 ctgactcaaa ctccactatt cctgttcctg actgtcagga actgttggaa actactgaaa 1440
 ctggccgacc tgatcttcaa aatgtgccc taggaaaggg ggatgccacc atgttcacag 1500
 acagtagcag ctctctcgag aagggactac gaaaggccgg tgcagctgtt accatggaga 1560
 cagatgtgtt gtgggtcag gctttaccag caaacacctc agcacaacaa gctgaattga 1620
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 cagcaggtgg ctgtaatcca ctgtaaagga catcaaaagg aaaacacggc tgttgcccg 1800
 ggtaaccaga aagctgattc agcagctcaa gatgcagtgt gactttcagt cagcctcta 1860
 aacttgctgc ccacagctctc ctttccacag ccagatctgc ctgacaatcc cgcatactca 1920
 acagaagaag aaaactggcc tcagaactca gagccaataa aaatcaggaa ggttggtgga 1980
 tcttctctga ctctagaatc ttcatacccc gaactcttgg gaaaacttta atcagtcacc 2040
 tcatagctac caccattta ggaggagcaa agctacctca gctcctccgg agccgtttta 2100

agatccccca	tcttcaaagc	ctaacagatc	aagcagctct	cgggtgcaca	acctgcgccc	2160
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caggagaaaa	gtgggaatt	gactttacag	aagtaaaacc	acaccgggct	gggtacaaat	2280
accttctagt	actggttagc	accttctctg	gatggactga	agcattttgt	acccaaaacy	2340
aaactgtcaa	tagggtagtt	aagtttttac	tcaatgaaat	catccctcga	catgggctgc	2400
ctgtttgcca	tagggtctga	taatggaccg	gccttcgcct	tgtctatagt	ttagtcatgc	2460
agtaagggct	taaacattca	atggaagctc	cattgtgcct	atcgacccca	gagctctggg	2520
caagtagaac	gcataaactg	caccctaaaa	aacactctta	caaaattaat	cttagaatac	2580
ggtgtaaatt	gtgtaagtct	ccttccttta	gccctactta	gagtaagggt	cactccttac	2640
tgggctgggt	tcttaccttt	tgaaatcatg	tatgggaggg	tgctgcttat	cttgccctaa	2700
ctaagagatg	cccaattggc	aaaaatatca	caactaatt	tattacagta	cctacagtct	2760
ccccaacagg	tacaagatat	catcctgcc	cttgctcgag	gaaccatcc	caatccaatt	2820
cctgaacaga	cagggccctg	ccattcatcc	ccgccagggt	acctgttgtt	tgtaaaaaag	2880
ttccagagag	aaggactccc	tcctgcttgg	aagagacctc	acaccgtcat	cacgatgcc	2940
acggctctga	aggtggatgg	cattcctgcg	tggattcatc	actcccgcat	caaaaaggcc	3000
aacagagccc	aactagaaac	atgggtcccc	agggctgggt	cagggccctt	aaaactgcac	3060
ctaagttggg	tgaagccatt	agattaatcc	tttttcttaa	ttttgtaaaa	caatgcatag	3120
cttctgtcaa	acttatgtat	cttaagactc	aatataaccc	ccttgttata	actgaggaat	3180
caatgatttg	attcccccaa	aaacacaagt	ggggaatgta	gtgtccaacc	tggtttttac	3240
taacctgttt	tttagactct	ccctttcctt	taatcactca	gcttgtttcc	acctgaattg	3300
actctccctt	agctaagagc	gccagatgga	ctccatcttg	gctctttcac	tggtagccgc	3360
ttcctcaagg	acttaacttg	tgcaagctga	ctccacgac	atccaagaat	gcaattaact	3420
gataagatac	tgtggcaagc	tatatccgca	gttccbagga	attcgtccaa	ttgatcacag	3480
ccctctacc	cttcagcaac	caccaccctg	atcagtcagc	agccatcagc	atcgaggcaa	3540
ggccctccac	cagcaaaaag	attctgactc	actgaagact	tggtatgaca	ttagtatttt	3600
tagcagtaaa	gttttttttt	ctttttcttt	ctttttttct	cgtgcc		3646

<210> 228

<211> 419

<212> DNA

<213> Homo sapien

<220>

<221> misc feature

<222> (1) (1) (419)

<223> n = A,T,C or G

<400> 228

taagagggta	caagatctaa	gcacagcgt	caatgcagaa	cacagaacgt	agcctggtaa	60
gtgtgttaag	agtgggaatt	tttggagtac	agagtaaggc	acctaacctt	agotgggggt	120
tgggtacggg	ccagatggc	ttacagaaga	aagtgtcttg	agatgagttt	ttaagaatga	180
ataaggatag	acacaagtga	ggactgacct	ggcagtggtg	aatggtggtg	ggcaaaaaac	240
ttcgcatgta	tggaaaactg	acgtacagga	atgaagaatg	agactgtgtg	gtgtttaatg	300
agctgcaaat	actaatttta	tcctgaaagt	tttgaagagt	taactaaaaa	gtatttttta	360
gtaaggaaat	aacctacat	ttcagggtta	ctgtttgttt	anatattgaa	ggtgcccaa	419

<210> 229

<211> 148

<212> DNA

<213> Homo sapien

<400> 229

aagagggtac	ctgtatgtag	ccatgggtgc	aatgagagac	tgattactac	ctgctggaga	60
ttgtttaagt	gagttaatat	attaaggata	aagggagcca	ggttttttga	ctgttggaga	120
aggaaattac	agatattgaa	ggtcccaa				148

<210> 230
 <211> 257
 <212> DNA
 <213> Homo sapien

<400> 230

```

taagagggtg cmaaaaaaaaa aaatagaac gaatgagtaa gacctactat ttgatagtac      60
aacagggtga ctatagtcaa tgataactta attatacatt taacatagag tgtaattgga      120
ttgtttgtaa ctggaaggat aaatgcttga gaggatggat accccattct ccatgatgta      180
cttatttcac attacatgcc tgtatcaaag catctcatat accctataaa tatgtacacc      240
tactatgtac cctotta                                     257
  
```

<210> 231
 <211> 260
 <212> DNA
 <213> Homo sapien

<400> 231

```

taagagggtg cgggtatttg ctgatgggat ttttttttct ttctttttct ttggaaaaca      60
aaatgaaggc cagaacaaaa ttattgaaca aaagacaggg actaaatctg gagaaatgaa      120
gtcccttacc ctgactacca ttctattcta tctaccttc cagtctaggt taggagaata      180
gggggtggag gggatttacc tcatcacagt atatttaaag caactctgca tgtgtgccag      240
aagtcctatg taccctotta                                     260
  
```

<210> 232
 <211> 596
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(596)
 <223> n = A,T,C or G

<400> 232

```

tgctcctctt gccttaccaa ccacaaatta gaaccataat gagatgtcac ctcatacctg      60
gtgggattaa cattatttaa aaatcagaa gtattgacaa gtagtggaag aaattagaac      120
atctgtgcac tgttggtggg aatgtaaaaa aggtgtggcc actatgggta acagcatgaa      180
ggttcctcaa aaaaaatttt ttttaattta ctctatgac gatcttgagg ttgtttatgc      240
aaaagaactg aaatcaggat tttaggaaa tttcacctt cccacatcca tttctgcttt      300
attcataata ctcaagagat ggaacacacc taatgtccc tcccgggatg aatggataaa      360
cacagtgtgg tatatgcata caatggaata ttatttagtc tttaaaaga aaaattctat      420
catatactac aacttanatn aaccttgagg acacaatgct nagtgaaata agccacggaa      480
ggacgaatac tgcattatct ccttatatga agtatctaaa gtggtcaaac tcttanagca      540
naaagtaaaa atgggtggtt gccanacagt tggttaggcn agaaganaan cctant      596
  
```

<210> 233
 <211> 96
 <212> DNA
 <213> Homo sapien

<400> 233

```

tcttctgaag acctttcggc actcttaagc tctgtggttg taaggcaaga ggagcgttgg      60
taaggcaaga ggagcgttgg taaggcaaga ggagca                                     96
  
```

<210> 234
<211> 313
<212> DNA
<213> Homo sapien

<400> 234
tgtaagtcga gcagtgtgat gataaaactt gaatggatca atagtggctt cttatggatg 60
agcaaagaaa gtatgttctt gtgatggaat ctgctcctgg caaaaatgct gtgaacgttg 120
ttgaaaagac aacaaagagt ttagagtagt acataaattt agaatagtac ataaaacttag 180
aatagtacat aaacttagta cataaataat gcacgaagca ggggcagggc ttgagagaat 240
tgacttcaat ttggaaagag tatctactgt aggttagatg ctctcaaaca gcatcacact 300
gctcgactta caa 313

<210> 235
<211> 550
<212> DNA
<213> Homo sapien

<400> 235
aacgaggaca gatcctttaa aagaatgttg agtgaaaaaa gtatgaaata agataatctct 60
caaagtcacg tagcattatt taaacatttt caaaaaatac actgataaaa attttgtaca 120
tttcccaaaa atacatatgg aagcacagca gcatgaatgc ctatgggrrt gaggataggg 180
gttgggagta gggatgggga taaaggggga aaataaaacc agagaggagt cctacacatt 240
tcatgaacca ggaggtataa ttatttcaac tatttgtacc wgaagtccag aaagagtggga 300
ggcagaaggg ggagaagagg gcgaagaaac gtttttggga gaggggtccc aagagagaga 360
ttttcgcat gtggcgctac atacgttttt ccaggatgcc ttaagctctg caacctatct 420
ttctcatcac taatattaga ttaaaccttt tgaagacagc gtctgtggtt tctctaactc 480
agctttccct ccgtgtcttg cacacagtag ctgttttaca agggttgaac tgactgaagt 540
gagattatc 550

<210> 236
<211> 325
<212> DNA
<213> Homo sapien

<400> 236
tagactgact catgtccctt accagagtag ctagaattaa tagcacaagc ctctacacct 60
aggaactcac tattgaatac ataaatggaa tttattcagc cctaaagaat ttggaaggaa 120
attctgacat atgctaaaac atggatgaac cttgaagact ttatgataag caaaagaagc 180
cagtcataaa aggaaaaata ttgcatgatt ccacttatat gaggtaccta gtagtgcata 240
tttcatagaa acacaaaata gaatgggtgtt cgccaggggt tttgaggaaa aggggaatgac 300
aagttagggg acatgagtca gtcta 325

<210> 237
<211> 373
<212> DNA
<213> Homo sapien

<220>
<221> misc feature
<222> (1) T (373)
<223> n = A, T, C or G
<400> 237

tagactgact catgtccct atctactcaa catttccact tgaagtctga taggcattct 60
 agacttatct tgtcccaaag caaactcttt atttcttttc atcctagtct ttattttctg 120
 tgctgtctta cccatctcaa aagagtgcc aaatccacca agttgctgaa acagaaatct 180
 aagaaatct cttgattctt ctttttccca tctacttcac ttctaattca ttagtaata 240
 atctgtttca gaaaaccaa cacctcatgt tctactcat aagggggagt tgaacaatga 300
 gaacacacag acacagggag gggaacatca cacaccagg cccgtcagg agtangggac 360
 atgagtcagt cta 373

<210> 238
 <211> 492
 <212> DNA
 <213> Homo sapien
 <220>
 <221> misc_feature
 <222> (1) ... (492)
 <223> n = A,T,C or G

<400> 238

tagactgact catgtccct ataatgctcc caggcatcag aaagcatctc aaactggagc 60
 tgacaccatg gcagagggtt caggtaagtc acaaaagggg tctaaagaa ttgcccctca 120
 atatcagagt gattagaaga agtgagaca gctaccaag ttaacatat gcgagataaa 180
 aaaaatatgg cacttgtgaa cacacactac aggaggaaaa taaggaacat aatagcatat 240
 tgtgtctatta tgatgatgaa gaacctctct anaagaaaac ataaccaag aaacaaagaa 300
 aattcctgcn aatgtttaat gctatagaag aaattaacaa aaacatatat tcaatgaatt 360
 cagaaaagtt agcagggtcan aagaaaacaa atcaaagacc agaataatcc cattttagat 420
 tgtcgagtaa actanaacag aaagaatacc actggaaatt gaattcctac gtangggaca 480
 tgantcanc ta 492

<210> 239
 <211> 482
 <212> DNA
 <213> Homo sapien
 <220>
 <221> misc_feature
 <222> (1) ... (482)
 <223> n = A,T,C or G

<400> 239

tggaagat ttaatgatgg gcaacttgct gtttacttcc tacatatccc atcatcttct 60
 gtattttttt aaataacttt tttttggatt tttaaagtaa ccttattctg agaggtaaca 120
 tggattacat acttctaagc cattaggaga ctctatgtta aacaaaagg aaatgttact 180
 agatcttcat ttgatcaata ggatgtgata atcatcatct ttctgctcta atggaaaagt 240
 actanaaaca tggaaccata atcttagatg aacaacgtta gaatttgac taattctacg 300
 gaatttcagt aattcggcaa atgtcgggca gtgacacaac atttcatgac ggggacgcat 360
 ctaccaactt ctggcgataa gggccaccct tccctctgta cttacagtcc catttcatac 420
 acagtctttg attaaatatt cacatttttt ctctacctaa agaccttcaa gaccagtacg 480
 ta 482

<210> 240
 <211> 519
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1) ... (519)
 <223> n = A,T,C or G
 <400> 240
 tgtatcgacg tagtgggtctc cccatgtgat agtctgaaat atagcctcat gggatgagag 60
 gctgtgcccc agcccgacac ccgtaaaggg tctgtgctga ggtggattag taaaagagga 120
 aagccttgca gttgagatag aggaagggca ctgtctcctg cctgcccctg ggaactgaat 180
 gtctcggtat aaaacccgat tgtacatttg ttcaattctg agataggaga aaaaccaccc 240
 tatggcggga ggcgagacat gttggcagca atgctgcctt gttatgcttt actccacaga 300
 tgtttgggcg gagggaaaca taaatctggc ctacgtgcac atccaggtat agtacctccc 360
 tttgaactta attatgacac agattccttt gctcacatgt ttttttgctg accttctcct 420
 tattatcacc ctgctctcct accgcattcc ttgtgctgag ataatgaaa taatatcaat 480
 aaaaacttga nggaactcgg agaccactac gtcgataca 519

<210> 241

<211> 771

<212> DNA

<213> Homo sapien

<220>
 <221> misc_feature
 <222> (1) ... (771)
 <223> n = A,T,C or G
 <400> 241
 tgtatcgacg tagtgggtctc cactcccgcc ttgacggggc tgctatctgc cttccaggcc 60
 actgtcacgg ctcccggtga gaagtcactt atgagacaca ccagtgtggc cttgttggct 120
 tgaagctcct cagaggaggg tgggaacaga gtgaccgagg gggcagcctt gggctgacct 180
 aggacgggtca gcttgggtccc tccgccaac acgagagtgc tgctgcttgt atatgagctg 240
 cagtaataat cagcctcgtc ctcagcctgg agcccagaga tggtcaggga ggcctgttg 300
 ccnacttgg agccagagaa gcgattagaa acccctgagg gccgattacc gacctcataa 360
 atcatgaatt tgggggcttt gcctgggtgc tgttgggtacc angagacatt attataacca 420
 ccaacgtcac tgctggttcc antgcaggga aaatggttga tcnaactgtc caagaaaacc 480
 actacgtcca taccaatcca ctaattgcn gccgcctgca ggttcaacca tattggggaa 540
 naactcccn ccgcggttg ggattgncat naaccttga aattttttcc tattanttgt 600
 cccctaaaa taaaccttg gcnntaatc cattgggtcc atancttntt tncctggttt 660
 ttaaaanttg tttatccgc cncctnaatt ccccccaac tttccaaaac ccgaaacct 720
 tnaaattnt tnaaacctc ggggggtccc nnaattnnan ttnaantcnc c 771

<210> 242

<211> 167

<212> DNA

<213> Homo sapien

<400> 242
 tgggcaacct caatatcggt ctcacgata acatcacgt gctgatgctg ctgttgctgg 60
 tctctctag gaacctctgg attttcaaat tctttgagga attcatocaa attatctgcc 120
 tctctcctt tctctcttt tctaaggtct tctggtacaa gcggtca 167

<210> 243

<211> 338

<212> DNA

<213> Homo sapien

<400> 243
 ttgggcacct tcaatatcta ctgatctaaa tagtgtggtt tgaggcctct tgttcttggc 60
 taaaaatect tggcaagagt caatctccac tttaaatag aggtaaaaat cttacaatgg 120
 atattcttga caagctagc atagagacag caattttaca caaggatttt ttcacctgtt 180
 taataacagt ggttttctta caccataggt gtgccacca gggaggagt cagagtgtga 240
 gaaacaaatt aagatactga agacaacact acttaccatt tcccgtatag ctaaccacca 300
 gttcaactgt acatgtatgt tcttatgggc aatcaaga 338

<210> 244
 <211> 346
 <212> DNA
 <213> Homo sapien

<400> 244
 tttttggctc ccatacagca cactctcatg ggaaatgtct gttctaaggt caaccataa 60
 tgcaaaaatc atcaatatac ttgaagatcc ccgtgttaagg tacaatgtat ttaattattat 120
 cactgatata atgatccaa taccagtttt agtctggcat tgaatcaaat cactgttttt 180
 gttgtataaa aagagaaata tttagcttat atttaagtac catattgtaa gaaaaaagat 240
 gcttatcttt acatgctaaa atcatgatct gtacattggt gcagtgaata ttactgtaaa 300
 agggagaag gaatgaugao gagctaagga tattgaaggt gcccaa 346

<210> 245
 <211> 521
 <212> DNA
 <213> Homo sapien
 <220>
 <221> misc_feature
 <222> (1) ... (521)
 <223> n = A,T,C or G

<400> 245
 accaatccca caggatact gagggacaag tatatcatcc catttcatcc ctacagcagc 60
 aacttcatga ggcaggagtt attagtccca ttttacagaa gaggaactg agacttaggy 120
 agatcaagta atttgccag gtgcacaaat tagtgataga gccagggtt gaagcgacgt 180
 ctgtcttaag ccaatgaccc ctgcagatta ttagagcaac tgttctccac aacagtgtaa 240
 gcctettgct anaagctcag gtccacaagg gcagagattt ttgtctgttt tgctcattgc 300
 tcttcccca ttgcttagag cagggtctgc cacgaancag gttctcaatg catagttatt 360
 aatgtatat aagagcaaac atatgttaca gagaacttgc tgtatgcttg tcacttacat 420
 gaatcacctg tganatgggt atgcttgctt cccantgttg cagatnaaga tattgaangt 480
 gcccaaatca ctanttgctg ggcctgcan gtccancata t 521

<210> 246
 <211> 482
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1) ... (482)
 <223> n = A,T,C or G

<400> 246
 tggaaaccaat ccaaatccc atcaatgata gactggataa agaaaatttg gcacatgttc 60

accatgaaat actatgcagc cataaaaaag gatgagttca tatectttgc agggacatgg 120
 atgaagctgg agaccatcat tctcagcaaa ctaacaaggg aacagaaaac caaacactgc 180
 atgtttctac tcttaagtgg gagctgaaca atgagaacac atggacacag ggaggggaac 240
 atcacacagt ggggcctgct ggtgggtagg ggtctagggg agggatagca ttaggagaaa 300
 tacctaattg agatgacggg tggatgggtg cagcaaacca ccatgacacg tgtatagcta 360
 tgaacaaaac ctgcatgttc tgcacatgta cccagaaact taaagtgtta ataaaaaat 420
 taagaaaaaa gttaagtatg tcatagatac ataaaatatt gtanataattg aaggtgccca 480
 aa 482

<210> 247
 <211> 474
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1) ... (474)
 <223> n = A, T, C or G
 <400> 247
 ttcgatacag gcacagagta agcagaaaaa tggctgtggt ttaacgaagt gactacagtt 60
 aagtgaagaga ggggcagaga agacaagggc atatgcaggg ggtgattata acaggtgggt 120
 gtgctgggaa gtgagggtag tggggatga ggaacagtga aaaagtggca aaaagtggta 180
 agatcagtga attgtacttc tccagaattt gatttctggn ggagtcaa atactatccag 240
 tttggggat catanggcaa cagttgaggt ataggaggta gaagtcncag tgggataatt 300
 gaggttatga anggtttggt actgactggt actgacaang tctgggttat gaccatggga 360
 atgaatgact gtanaagcgt anaggatgaa actattccac ganaaagggg tccnaaaact 420
 aaaaannnaa gnnnnngggg aatattattt atgtggatat tgaangtgcc caaa 474

<210> 248
 <211> 355
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1) ... (355)
 <223> n = A, T, C or G
 <400> 248
 ttcgatacag gcaaacatga actgcaggag ggtgggtgag atcatgatgt tgccgatggt 60
 ccggatggnc acgaagacgc actgganac gtgcttagct ccttttgctc tgttgatggc 120
 cctgagggga cgcaggaccc ttatgacctt cagaatcttc acaacgggag atggcactgg 180
 attgantccc antgacacca gagacacccc aaccaccagn atatcantat attgatgtag 240
 ttctctgtaga nggccccctt gtggaggaaa gctccatnag ttggtcatct tcaacaggat 300
 ctcaacagtt tccgatggct gtgatgggca tagtcatant taacntgtn tcgaa 355

<210> 249
 <211> 434
 <212> DNA
 <213> Homo sapien

<400> 249
 ttggattggt cctccaggag aacaagggga aaaaggtgac cgagggctcc ctggaactca 60
 aggatctcca ggagcaaaag gggatggggg aattcctggt cctgctggc ccttaggtcc 120

```

acctggctcct ccaggcttac caggctcctca aggcccaaaag ggtaacaaag gctctactgg 180
acccgctggc cagaaagggtg acagtgggtct tccagggcct cctggggcct cagggtccacc 240
tggtgaagtc attcagcctt taccaatctt gtccctccaaa aaaacgagaa gacatactga 300
aggcatgcaa gcagatgcag atgataatat tcttgattac tcggatggaa tggagaaat 360
atttggttcc ctcaattccc tgaaacaaga catcgagcat atgaaatttc caatgggtac 420
tcagaccaat ccaa 434

```

<210> 250

<211> 430

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)..(430)

<223> n = A,T,C or G

<400> 250

```

tggattggtc acatggcaga gacaggatte caaggcagtg agaggaggat acaatgcttc 60
tcactagtta ttattattta ttttattttt gagatgaagt ctcgctttgt ctcccaggct 120
ggagagcggg ggtgcgatct tggctctctg caacccccgc ctcaagcaat tctcctgtct 180
tagcctcgcg ggtagatgga attacaggcg cccaccgcca tgcccaacta atttttttgt 240
gtcttcagta gagacagggt ttcgccatgt tgggcaggct ggtcttgaac tcttgacctc 300
nagtgatctg cctcctcgg cctcacaaag tgctggaatt acaggcatgg gctgctgcac 360
ccagtcaact tctcactagt tatggcctta tcattttcac cacattctat tggcccaaaa 420
aaaaaaaaan 430

```

<210> 251

<211> 329

<212> DNA

<213> Homo sapien

<400> 251

```

tggtaactcca ccatyatggg gtcaaccgcc atcctcgccc tctcctggc tgttctccaa 60
ggagtctgtg cagaggtgca gctgrtgacg tctggagcag aggtgaaaaa gtccggggag 120
tctctgaaga tctcctgtaa gggttctgga tacaccttta agatctactg gatcgctgg 180
gtgcgccagt tgcccggaag aggcctggag tggatggggc tcatctttcc tgatgactct 240
gataccagat acagcccgtc cttccaaggc caggtcacca tctcagtcga taagtccatc 300
agcaccgct atctgcagtg gattacca 329

```

<210> 252

<211> 536

<212> DNA

<213> Homo sapien

<400> 252

```

tggtaactcca ctacgcccga ccttaattaa gaattaagag ggaacctatt actattctcc 60
caggctcctc tgctctaacc aggtctctgg gacagtatta gaagaggatg tctcaacaag 120
tatgtagatc ctgtactggc ctaagaagtt aaactgagaa tagcataaat cagaccaaac 180
ttaatggctg ttgagacttg tgcctggag cagctgggat aggaaaactt ttgggcagca 240
agaggaagaa ctgctggaa gggggcatca tggtaaaaat tacaagggga acccacacca 300
ggcccccttc ccagctctca gcctagagta ttagcatttc tcagctagag actcacaact 360
tccttgctta gaatgtgcca ccggggggag tccctgtggg tgatgaggct ctcaagagt 420
agagtggcat cctatcttct gtgtgcccac aggagcctgg cccgagactt agcagggtga 480
gtttctggtc caggctttgc ccttgactca ctatgtgacc tctggtggag taccaa 536

```

<210> 253
<211> 507
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)... (507)
<223> n = A,T,C or G

<400> 253

```
ntgttgcgat cccagtaact cgggaagctg agggcggagg atcacctgag ctcaggaggt    60
tgaggccgca gtgagccggg accacgccac tacactccag cctggggcat agagtgagac    120
cctccaagac agaaaagaaa agaaaggaag ggaaagggaa agggaaaagg aaaaggaaaa    180
ggaaaaggaa aaggaaaaga caagacaaaa caagacttga atttggatct cctgacttca    240
attttatgtt cttttacac cacaattcct ctgcttacta agatgataat ttagaaaccc    300
ctcgttccat tttttacagc aagctggaag tttggtcaag taattacaat aatagtaaca    360
aatttgaata ttatatgcca ggtgttttct attcctgctc tcaacttaatt ctcaccactc    420
tgatataaat acaattgctg ccgggtgtgg tggctcatgc ctgtaattcc ggcactttgg    480
gagaccgagg tgggaggatg gcaacaaa
```

<210> 254
<211> 222
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)... (222)
<223> n = A,T,C or G

<400> 254

```
ttggattggt cactgtgagg aagccaaate ggatccgaga gtctttttct aaaggccagt    60
actggccaca cttttctctg ccgccttctc caaagctgaa gaacacacaga gcaaggcgct    120
tctgttttac tcccgaatgg taactccaaa ccatagatgg ttagctnccc tgctcatett    180
tccacatccc tgctattcag tatagtccgt ggaaccaatcc aa
```

<210> 255
<211> 463
<212> DNA
<213> Homo sapien

<400> 255

```
tgttgcgac cataaatgct gaaatggaaa taaacaacat gatgaggagg gattaagttg    60
gggaggggagc acattaaggt ggccatgaag tttgttgga gaagtgactt ttgaacaagg    120
ccttggtgtt aagagctgat gagagtgtcc cagacagagg ggccactggt acaatagacg    180
agatgggaga gggcttgga ggtgtgcaaa atagggaagg gtttgttctg gtatgagtct    240
agtgaacaca gaggcgagag gccttggtgg gtgagctggg agagtattgc agaataacat    300
taggccctgt gggggactgt agactgtcag caataatcca cagtttggat tttattctaa    360
gagtgatggg aagcgttga aaggggggta agcaaggagt gaaattatca gatttacagt    420
gataaaaaata aattggtctg gctactgggg aaaaaaaaaa aaa
```

<210> 256
<211> 262

<212> DNA
<213> Homo sapien

<400> 256

```

ttggattggt caacctgctc aactctacyt ttctccttc ttcctaaaaa attaatgaat    60
ccaatacatt aatgccaaaa cccttggggt ttatcaatat ttctgttaaa aagtattatc    120
cagaactgga cataatacta cataataata cataacaacc ccttcacctg gatgcaaaca    180
tctattaata tagcttaaga tcactttcac ttacagaag caacatcctg ttgatgttat    240
tttgatgttt ggaccaatcc aa                                         262

```

<210> 257
<211> 461
<212> DNA
<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(461)

<223> n = A,T,C or G

<400> 257

```

gnggnnnnnn nnncattcg actcngttcc cntggtancc ggtcgacatg gcgcggggat    60
taccgcttgt nactgggggt gtatggggga ctatgaccgc ttgtagctgg ggggtgatgg    120
gggactatga ccgcttgtag mtggkggtgt atgggggact atgaccgctt gtcgggtggg    180
cggataaacc gacgcaaggg acgtgatcga agctgcgttc ccgctcttcc gcacggttag    240
ggatcatgga cagcaatata cgcattcgyt tgaaggcgtt cgaccatcgc gtgctcgatc    300
aggcgaccgg cgacatcgcc gacaccgcac gccgtaccgg cgcgctcatc cgcggtccga    360
tcccgccttc caccgcgcatc gagaagtcca cggtaaccgg tggcccgcac gtcgacaaga    420
agtcgcgcga gcagttcgag gtgcgtacct acaagcggtc a                                         461

```

<210> 258

<211> 332

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(332)

<223> n = A,T,C or G

<400> 258

```

tgaccgcttg tagctggggg tgtatggggg actacgaccg cttgtagctg ggggtgtatg    60
ggggactatg accgcttgta gctgggggtg tatgggggac tatgaccgct tgtagctggg    120
gggtgtatgg ggactaggac cgcttgtagc tgggggtgta tgggggacta tgaccgcttg    180
tagctggggg tgtatggggg actacgaccg cttgtagctg ggggtgtatg ggggactatg    240
accgcttgta nctgggggtg tatgggggac tatgaccgct tgtgctgcct gggggatggg    300
aggagagttg tggttgggga aaaaaaaaaa aa                                         332

```

<210> 259
<211> 291
<212> DNA
<213> Homo sapien

<220>

<221> misc_feature

<222> (1) ... (291)
<223> n = A,T,C or G

<400> 259
taccgcttgt gaccgcttgt gaccgcttgt gaccgcttgt gaccgcttgt gaccgcttgt 60
gaccgcttgt gaccgcttgt gaccgcttgt gaccgcttgt gaccgcttgt gaccgcttgt 120
gaccgcttgt gaccgcttgt nachgggggt gtctggggga ctatgannga ntgthactgg 180
gggtgtctgg gggncatga nngantgtna cnygggggtgt ctgggggact atganngact 240
gtgcnnctcg ggggacnga ggagantngn ggntagnat ggtnhggan a 291

<210> 260
<211> 238
<212> DNA
<213> Homo sapien

<400> 260
taagagggtta ctggttaaaa tacaggaaat ctggggtaat gaggcagaga accaggatac 60
tttgaggtca gggatgaaaa ctagaatttt tttctttttt tttgcctgag aaacttgctg 120
ctctgaagag gcccatgtat taattgcttt gatcttcctt ttcttacagc cctttcaagg 180
gcagagccct ccttatcctg aaggaatctt atccttagct atagtatgta cctctotta 238

<210> 261
<211> 746
<212> DNA
<213> Homo sapien
<220>
<221> misc_feature
<222> (1) ... (746)
<223> n = A,T,C or G

<400> 261
ttgggcacct tcaatatcaa tagctaacat ttattgagtgt tttatcgtat cataaaacac 60
tggttctaagc ctttaaacgt actaattcat ttaatgctca taattacttt agaaggtggg 120
tactagtatt agtctcattt acagatgcaa catgcaggca cagagaggtt aattaacttg 180
cccaaggtaa cacagctaaag aaatagaaaa aatattgaat ctggaaaagt gggcttcttg 240
gtaaccaca gagtcttcaa tgagcctggg gcctcactca gtttgctttt acaaagcgaa 300
tgagtaacat cacttaattc agtgagtagg ccaaatggag gtcagctacg agtttctgct 360
gttcttgcag tggactgaca gatgtttaca acgtctggcc atcagtwaat ggactgatta 420
tcattgggaw gtgggtgggc tgaatgttgg ccagtgaagt ttattcawgc catattttta 480
tgtttaggat gacttttggc tggctctagg gcaagctctg tctgscacgg aacacagaat 540
wacacaggga cccctcaat ttctggtgtg yctagaacca tgaaccactg gttgggggaa 600
caagcgggtca aaacctaagt gcggccggct ggcaggytcc acccatatgg ggaaaactcc 660
cnacgcgttt ggaatgcctn agctngaatt attctaanag ttgtccnctt aaaattagcc 720
tgggcgttaa tcangggctn naagcc 746

<210> 262
<211> 588
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1) ... (588)
<223> n = A,T,C or G

<400> 262

tgaccgcttg	tcattctcaca	tggggctcctg	cacgcttttg	cctttgtagg	aaacctgaca	60
tttgtctggt	ttttctttct	ttttccttc	ccatatectc	ctaatttacg	tttgacttgt	120
ttgctgagga	ggcaggagct	agagactgct	gtgagctcat	aggggtggga	agtttatcct	180
tcaagtcccg	cccactcctc	actgcttctc	accttccct	gaccaggctt	acaagtgggt	240
tcttgctgc	tttcccttg	gacccaacaa	gcccctgtaa	tgagtgtgca	tgactctgac	300
agctgtggac	tcagggtcct	tggctacagc	tgccatgtaa	aatatctcat	ccagttctcg	360
caaattgtta	aaataaccac	atttcttaga	ttccagtacc	caaatcatgt	ctttacgaac	420
tgctcctcac	accagaagt	ggcacaataa	ttcttgggga	attattactt	tttttttct	480
ctctnttnc	gnnnngnnng	gnnnngccag	gaattaccac	nttggaagac	ctggccngaa	540
tttattatan	aggggagcgc	attntttttc	ctaacacaaa	gcgggtca		588

<210> 263

<211> 730

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1) ... (730)

<223> n = A,T,C or G

<400> 263

tttttttttt	tttggcctga	gcaactgaaa	ttatgaaatt	tccatatact	caaaagagta	60
agactgcaaa	aagattaaat	gtaaaagttg	tcttgtatac	agtaatgttt	aagatacctt	120
ttanatttat	aaatggaaaa	ttagggcatt	tggatataca	agttgaaaat	tcaggagtga	180
ggttgggctg	gctgggtata	tactgaaaac	tgtcagtaca	cagatgacat	ctaaaaccac	240
aaatctgggt	ttatttttagc	agtgatatgt	gtcactccca	caaaagcctt	cccaattggc	300
ctcagcatac	acaacaagtc	acctccccac	agccctctac	acataaacia	attccttagt	360
ttagttcagg	aggaaatgcg	cccttttctt	tccgtcttag	gtgaccgcaa	ggcccagttc	420
tcgtcaccaa	gatgttaagg	gaagtctgcc	aaagaggcat	ctgaaaggaa	ataaggggaa	480
tgggagtgc	cacaaaggaa	agccaaggan	aaactttgga	gaccgtttct	aganccctgg	540
catttcacaa	caaaactcng	gaacaaacct	tgtctcatca	atcatttaag	cccttcgttt	600
ggannagact	ttctgaactg	ggcgtgaac	ataancctca	ttgaatgtct	tcacagctctc	660
ccagctgaag	gcacaccttg	ggccagaagg	ggaatcttcc	aggtcctcaa	nacagggtctc	720
gccttttgnc						730

<210> 264

<211> 715

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1) ... (715)

<223> n = A,T,C or G

<400> 264

tttttttttt	tttggccagt	atgatagtct	ctaccactat	attgaagctc	ttaggtcatt	60
tacacttaat	gtggttatag	atgctgttga	gcttacttct	accacottgc	tatttctccc	120
gtctcttttt	tgttcctttt	ctcttctttt	cctcccttat	tttataattg	aatttttttag	180
gattctattt	tatatagatt	tatcagctat	aacactttgt	attcttttgt	tttgtgggtc	240
ttctgtcatt	tcaatgtgca	tcttaaacctc	atcacaatct	attttcaaat	aatatcatat	300
aaccttacat	ataatgtaag	aatctaccac	catatatttc	catttctccc	ttccatccta	360

tgtntgtcat atttttctct ttatatatgt tttaaagaca taatagtata tgggaggttt 420
 ttgcttaaaa tgtgatqaat attccttcaa ngaaacgtaa aaattcaaaa taaatntctg 480
 tttattctca aatnnaccta atatttctcta ccatntctna tacntttcaa gaattctgaag 540
 gcattgggtt tttccggctt aagaacctcc tctaaagcac tctaagcaga attaagtctt 600
 ctgggagagg aattctccca agcttggggc ttnanntgta ctccnthang gttaaaatttt 660
 ggccgggaaa tagaaattcc aagttaacag gntanttttt ntntntnttn tcncc 715

<210> 265

<211> 152

<212> DNA

<213> Homo sapien

<400> 265

tttttttttt tttcccaaca caaagcacca ttatctttcc tcacaatttt caacatagtt 60
 tgattcccat gaagaggta tgatttctaa agaaaacatg gctactatac tatcaatcag 120
 ggtaaactct tttttttttg agacggagtt ta 152

<210> 266

<211> 193

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(193)

<223> n = A,T,C or G

<400> 266

taaactccgt ccccttctta atcaatatgg aggtaacca ctccacatta ccttcttttc 60
 aaggagctgt ttccgtaact gttgtgggta ttcacgacca ggcttctaaa cctcttaaaa 120
 ctccccaaatt ctggtgccaa cttggacaac atgctttttt tttttttttt tttttttttt 180
 gagacggagtt tta 193

<210> 267

<211> 460

<212> DNA

<213> Homo sapien

<400> 267

tgttgcatc ccttaagcat ggggtctatt aaaaaaatgg tggagaagaa aatacctgga 60
 atttacgtct tatctttaga gattgggaag accctgatgg aggacgtgga gaacagcttc 120
 ttcttgaatg tcaattccca agtaacaaca gtgtgtcagg cacttgctaa ggatcctaaa 180
 ttgcagcaag gctacaatgc tatgggattc tcccaggagg gccaatctct gagggcagtg 240
 gctcagagat gcccttcacc tcccatgac aatctgatct cggttggggg acaacatcaa 300
 ggtgtttttg gactccctcg atgccagga gagagctctc acatctgtga cttcatccga 360
 aaaacactga atgctggggc gtactccaaa gttgttcagg aacgcctcgt gcaagccgaa 420
 tactggcatg acccataaaa ggaggatgtg gatcgcaaca 460

<210> 268

<211> 533

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(533)

<223> n = A,T,C or G

<400> 268

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tggtgcatc cgttgataga atagcgacgt ggtaatgagt gcatggcacg cctccgactt 60
accttcgccc gtggggaccc cgagtacgtc tacggcgctg tcacttagag taccctctgg 120
acgcccgggc gcgttcgatt taccggaagc gcgagctgca gtgggcttgc gccccggcc 180
aaattctttg gggggtttaa ggccgcgggg aatttgaggt atctctatca gtatgtagcc 240
aagttggaac agtcgccatt cccgaaatcg ctttctttga atccgcaccg cctccagcat 300
tgccatcttc atcaacctga aggcacgcat aagtgcggtg tgtgtcttca gcagctccac 360
tccataacta gcgcgctcga cctcgtcttc gtacgcgcca ggtccgtgcg tgcgaattcc 420
caactccggt gagttgcgca tttcaagttt cgaactgtt cgcctccacn atttggcatg 480
ttcacgcatg acacggaata aactcgtcca gtaccgggaa tgggatcgca aca 533

```

<210> 269

<211> 50

<212> DNA

<213> Homo sapien

<400> 269

```

tttttttttt ttgcctgaa tttagctagag atctcctca caagcgggtca 50

```

<210> 270

<211> 519

<212> DNA

<213> Homo sapien

<400> 270

```

tggtgcatc caaataaccc accagcttct tgcacacttc gcagaagcca ccgtcctttg 60
gctgagtcac gtgaacggtc agtgcaagca gccgcgtgcc agagcagagg tgcagcatgc 120
tgcacaccag ctcagggtcg acctcctcca gcaggatgga caggatggag ctgccgtacg 180
tgtccaccac ctctggcac tcttcgcaca gggacttcgg cagcttcgag cacattttgt 240
caaaagcgtc gagtatttct ttctcagctc tgttgttgc aatcagcttg gtcacctcct 300
tcaccaggaa ttcacacacc tcacagtata catcagactt tgctgggacc tegtgtctct 360
taatgggctc caccagttcc agggcagggg tgacattctt ggaggccact ttggcgggga 420
ccagagtctg catgggcate tctttcacctc atcacagaa cccaaccagc gcacagatct 480
ccttgggttg catgtgcatc atcatctggg atcgcaaca 519

```

<210> 271

<211> 457

<212> DNA

<213> Homo sapien

<400> 271

```

tttttttttt ttggggcggc gaccggacgt gcactcctcc agtagcggct gcacgtcgtg 60
ccaatggccc gctatgagga ggtgagcgtg tccggcttcg aggagtcca cggggcgtg 120
gaacagcaca atggcaagac cattttcgcc tactttacgg gttctaagga cgccgggggg 180
aaaagctggt gccccgactg cgtgcagget gaaccagtcg taqgagagg gctgaagcac 240
attagtgaag gatgtgtgtt catctactgc caagtaggag aagagcctta ttgaaagat 300
caaataaatg acttcagaaa aaacttgaaa gtaacagcag tgcctacact acttaagtat 360
ggaacacctc aaaaactggt agaactctgag tgtcttcagg ccaacctggt ggaaatgttg 420
ttctctgaag attaagattt taggatggca atcaaga 457

```

<210> 272

<211> 102

<212> DNA
<213> Homo sapien

<400> 272

tttttttttt ttgggcaaca acctgaatac cttttcaagg etctgggttg ggctcaagcc 60
cgcagggggaatgtcaactgg ccagggtcaca gggcaattcaagaa 102

<210> 273

<211> 455

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(455)

<223> n = A,T,C or G

<400> 273

tttttttttt ttggcaatca acagggttaa gtcttcggcc gaagttaatc tegtgttttt 60
ggcaatcaac aggtttaagt cttcggccga agttaatctc gtgttttttg caatcaacag 120
gtttaagtct tcggccgaag ttaatctcgt gtttttggca atcaacaggt ttaagtcttc 180
ggccgaagtt aatctcgtgt ttttggcaat caacaggttt aagtcttcgg ccgaagttaa 240
tctcgtgttt ttggcaatca acagggttaa gtcttcggcc gaagttaatc tegtgttttt 300
ggcaatcaag aggtttaagt cttcggccga agttaatctc gtgttttttg caatcaacag 360
gtttaagtct tcggccgaan ttaatctcgt gtttttggca atcaacaggt ttaantcttc 420
ggccgaagtt aatctcgtgt ttttggcaat caana 455

<210> 274

<211> 461

<212> DNA

<213> Homo sapien

<400> 274

tttttttttt ttggccaata ccttgatga acatcaatgt gaaaatcttc ggtaaaatad 60
tggcaaacca aatccagcag cacatcaaaa agcttatcca ccattgatcaa gtgggcttca 120
tccctgggat gcaaggctgg ttcaacataa gaaaatcaat aaatgtaatc catcacataa 180
acagaaccaa agacaaaac cacatgatta tctcaataga tgcagaaaag gccttggaca 240
aattcaacag cccttcatgc taaacactct taataaacta gatattgatg gaatgtatct 300
caaaataaga agagctattt atgacaaacc cacagccaat atcatactga atgggcaaaag 360
actggaagca ttccctttga aaactggcac aagacaagga tgccctctct caccgtcct 420
attcaacata gtattggaag ttctggccag ggcaatcaag a 461

<210> 275

<211> 729

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(729)

<223> n = A,T,C or G

<400> 275

tttttttttt ttggccaaca ccaagtcttc cactggggag gttttattat gttttacaac 60
catgaaaaca taggaaggtg gctgttacag caaacatttc agatagacga atcggccaag 120

```

ctccccaac cccaccttca cagcctcttc cacacgtctc ccanagattg ttgtccttca 180
cttgcaaatt canggatgtt ggaagtngac atttnnagtn gcnggaacco catcagttaa 240
ncantaagca gaantacgat gactttgana nacanctgat gaagaacacn ctacnganaa 300
ccctttctnt cgtgttanga tctcnngtcc ntcaactaatg cggccccctg cnggtccacc 360
atttgggaga actcccccn cgttgatcc ccccttgagt ntccattct ngccccan 420
accngcttg ngngncantn cncctcnc cctgtttcc ctgngtnaa aatnngtttt 480
nccgcnccc naattcccac ccnaatcaca gcgaancng aaggccttcn naagtgttta 540
angcccnng gtttctctnt ntanttcag cctaccctcc cncctnnnt tncngttgg 600
tegcgcctg gncnccctn gttctcttt nnggnnaca cctngntcnn nggcnctcn 660
nnctnttcc tnnactagc tngcctntcc nnccgnggn ncanngcaca ttncnncnac 720
tntgtnncc 729

```

<210> 276

<211> 339

<212> DNA

<213> Homo sapien

<400> 276

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tgacctgaca ttagtagat acttaataaa ttttgtgga atgaatgat gaagtggagt 60
tacagagaaa aatagaaaag tacaattgt tgcagtgtt ttgaaggaaa attatgatct 120
ttcccaagt totgacttca ttctaagaca gggtagtat ctccatacat aattttactt 180
gcttttgaaa atcaaatgag ataacttatt tagattgata atttatttag actggctata 240
aactattaag tgtagcaa tatacatttt aatctcattt tccacctctt gtgatatagc 300
tatgtaggtg ttgactttaa tggatgtcag gtcaatccc 339

```

<210> 277

<211> 664

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1). 33(664) 339

<223> n = A,T,C,G

<400> 277

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tgacctgaca tccataacaa aatctttctc cattatatcc ttctagggga atttcttgaa 60
aagcatccaa aggaacaaa tgatggtaag accgtgccaa gtggggagca gacaccaaag 120
taagaccaca gattttacat tcaacaggta gctcacagta ctttgccga cactgtgggc 180
agaaatagcc tcctaattga agccctggct cagtattgcc atccaaatgc gccatgctga 240
aagagggttt tgcacctgg tcagatnaag aagcaatggt gtgctgagga aatcccatac 300
gaataagtga gcattcagaa cttgagctag caggaggagg actaagatga tgtgtgagca 360
actctttgta atggctttca tctaaaataa catggtacgt gccaccagtt tcacgagcaa 420
gtacagtga aacgcgaact tctgcagaca atccaaatac agatactcta attttagctg 480
cctttagggt cttgattaaa tcataaatat tagatggatc gcaagttgta aggntgctaa 540
aagatgatta gtacttctcg acttgatgt ccaggcatgt tgttttaaan tctgccttag 600
nccctgetta gggaatttt taaagaagat ggctctccat gttcanggtc aatcacnaat 660
tgcc 664

```

<210> 278

<211> 452

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1) ... (452)

<223> n = A,T,C or G

<400> 278

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tgacctgaca ttgaggaaga gcacacacct ctgaaattcc ttaggttcag aagggcattt 60
gacacagagt gggcctctga taattcatga aatgcattct gaagtcattc agaatggagg 120
ctgcaatctg ctgtgctttg ggggttgctt cactgtgctc ctggatatca cacaaaagct 180
gcaatccttc ttcttcaact aacattttgc agtattttgt gggattttta ctgagacat 240
gatacatagc ccatagtgcg cagagctgaa cctctggttg agagaagtgt ccaaggagcg 300
ggaaaaatgt cttgaaagat ctataggtca ccaatgctgt catcttaca cttgaacttg 360
gccaattctg tatggttgca tgcagatctt ggagaagagt acgctctgga aagtcacggg 420
atatccaaan ctgtctgtca gatgtcaggt ca 452
```

<210> 279

<211> 274

<212> DNA

<213> Homo sapien

<400> 279

```
tttttttttt ttgggaagg caaatctact ttgcaaaag ggtgctgctt gcacttttgg 60
ccactgcgag agcacaccaa acaaagtagg gaaggggttt ttatccctaa cggggttatt 120
ccctggttct gtgtcgtgtc cccattggct ggagtcagac tgcacatctt acactgaccc 180
aactggctac tgtttaaaat tgaatatgaa taattaggtt ggaaggggga ggctggttgt 240
tacgttaca gacgtgtttg ggcattgcag gtca 274
```

<210> 280

<211> 272

<212> DNA

<213> Homo sapien

<400> 280

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tacctgacat ggagaaataa cttgtagtat tttgcgtgca atggaatact atatgagggt 60
gaaaatgaat gaactagcaa tgcgtgtatc aacatgaata aatccccaaa acataataat 120
gttgaatgga aaagggtgagt ttcagaagga tatatatgcc ctctaaatcc atttatgtaa 180
acctttaaaa aactacatta tttatggtca taagtccatc cagaaaatat ttaaaaacct 240
acatgggatt gataactact gatgtcaggt ca 272
```

<210> 281

<211> 431

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1) ... (431)

<223> n = A,T,C or G

<400> 281

```
tttttttttt ttggcaata gcatgattta aacattggaa aaagtcaaat gagcaatgcg 60
aatttttatg ttctgtgaa taatcaaaag agtaggcaac attggttcct cattcttgaa 120
tagcattaat cagaaaatat tgcatagcct ctagcctcct tagagtaggt gtgctctctc 180
aaatatatca tagtcacaca gtttatttca tgtatatatt ctgcttgaat cacatagaca 240
tttgaatttg caacgcctga tgtaaatata taaattctta ccaatcagaa acatagcaag 300
aaattcaggg acttggtcac yatcagggtt tgacagcana tccctgtara aacactgata 360
```

cacactcaca cacgtatgca acgtggagat gtcgcyttww kkktywccwm rmrycrwecn 420
aatcacttan n 431

<210> 282
<211> 98
<212> DNA
<213> Homo sapien

<400> 282
attcgattcg atgcttgagg ccaggagttc aagactgcag tgagccactg cacttcaggc 60
tggacaacag agcgagtccc tgtgccaata aaaaaaaaa 98

<210> 283
<211> 764
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1) (764)

<223> n = A, T, C or G

<400> 283
tttttttttt ttcgcaagca cgtgcacttt attgaatgac actgtagaca ggtgtgtggg 60
tataaactgc tgtatctagg ggcaggacca agggggcagg ggcaacagcc ccagcgtgca 120
gggccascac tgcacagtgg astgcaaagg ttgcaggcta tgggaggcta ctavtaaccc 180
cgttttttct gtattatctg taacataata tggtagactg tcacagagcc gaatwccart 240
hacagatga atccaawgt caygaggatg ccasaatca gggcccasat sttcaggcac 300
ttggcggtgg gggcataagc ctgkgcccgc gtcacgtcsc caaccwtcty cctgtcccta 360
cmcttgawtc cncncttnn nntnccntna tntgcccgc cncctcctng ngtcaaccng 420
natctgact anctcctcn ccccttntgg antctctcc tccaantaan nttatccttn 480
acnccccct cnccttccc ctncncccn tnatccngn nccnctatca ntentnccct 540
cncntnctn cnnatcgttc cncctntaa ctacncttn naccnncct cactnatncc 600
ngnnantttt ttccttccct ccnaccgcn tgcgtgcgcc cgtctnccct nnnctnccna 660
cccnactttt atttaccctt ncaccctagc nctctacttn acccancnc tcttacctcc 720
ngnccaccc nncctnctn nctnctctn tcnctcctt cccc 764

<210> 284
<211> 157
<212> DNA
<213> Homo sapien

<400> 284
caagtgtagg cacagtgatg aaagcctgga gcaaacacaa tctgtgggta attaacgttt 60
atttctcccc ttccaggaaac gtcttgcatg gatgatcaaa gatcagctcc tggtaacat 120
aaataagcta gtttaagata cgttccccta cacttga 157

<210> 285
<211> 150
<212> DNA
<213> Homo sapien

<400> 285
attcgattgt actcagacaa caatatgcta agtgggaagaa gtcagtcaca aaagaccaca 60
tactgtatga cttcatttac attaatgtgc cagaataggc aaatccgtag agacagaaag 120

tagatgagca gctgcctagg tctgagtaca 150

<210> 286
<211> 219
<212> DNA
<213> Homo sapien

<400> 286
attcgatttt tttttttttg gccatgatga aattcttact ccctcagatt ttttgtctgg 60
ataaatgcaa gtctcaccac cagatgtgaa attacagtaa actttgaagg aatctcctga 120
gcaaccttgg ttaggatcaa tccaatattc accatctggg aagtcaggat ggctgagttg 180
caggtcttta caagttcggg ctggattggg ctgagtaca 219

<210> 287
<211> 196
<212> DNA
<213> Homo sapien

<400> 287
attcgattct tgaggctacc aggagctagg agaagaggca tggaaacaaat tttccctcat 60
atccatactc agaaggaacc aacctgtctg acaccttaat ttcagcttct ggctctaga 120
actgtgagag agtacatttc tcttggttta agccaagaga atctgtcttt tggtaacttta 180
tatcatagcc tcaaga 196

<210> 288
<211> 199
<212> DNA
<213> Homo sapien

<400> 288
attcgatttc agtccagtc cagaaccac attgteaat actactctgt araagattca 60
tttgttgaaa ttcattgagt aaaacattta tgatccctta atatatgcca attaccatgc 120
taggtactga agattcaagt gaccgagatg ctagcccttg gggtcaagtg atccctctcc 180
cagagtgcac tggactgaa 199

<210> 289
<211> 182
<212> DNA
<213> Homo sapien

<400> 289
attcgattct tgaggctaca aacctgtaca gtatgttact ctactgaata ctgtaggcaa 60
tagtaataca gaagcaagta tctgtatatg taaacattaa aaaggtacag tgaaacttca 120
gtattataat cttagggacc accattatat atgtggtcca tcattggcca aaaaaaaaaa 180
aa 182

<210> 290
<211> 1646
<212> DNA
<213> Homo sapien

<400> 290
ggcagagga gaaatgtaat tccatatttt atttgaaact tattccatat ttttaattgga 60
tattgagtga ttgggttatc aaacaccac aaactttaat tttgttaaatt ttatatggct 120
ttgaaataga agtataagtt gctaccattt ttgataaca ttgaaagata gtattttacc 180

atctttaatc	atcttggaac	atacaagtcc	tgtgaacaac	cactctttca	cctagcagca	240
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 <212> DNA
 <213> Homo sapien
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 aagatctgga caagctccac agagctgccc tgggtgggta aagtcoccag aaaggatctc 240
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 catctggcct ctgccaatgg gaattcagaa gtagtaaac tctgctgga cagacgatgt 360
 caacttaatg tcttgacaa caaaaagagg acagctctga yaaaggcgt acaatgctag 420
 gaagatgaat gtgcgttaat gttgctggaa catggcactg atccaaatat tccagatgag 480
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 cttattttta aatattgtta ttttcaaaga agcattagag ggtacagttt ttttttttta 780
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 ttgccttgaa ataggtttta catgaaaact ccaagaaaag ttaaacaatgt ttcagtgaat 960
 agagatcctg ctctcttggc aagttcctaa aaaacagtaa tagatacgag gtgatgagcc 1020
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 <212> PRT
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 Glu Tyr Thr Ile Val His Ala Ser Phe Ile Ser Cys Ile Ser Ser Ser 35
 Leu Asp Gly Gln Gly Glu Arg Gln Gln Arg Gly His Phe Trp Arg 50
 Pro Gln Arg Leu Leu Cys Glu Asp Ala Trp Glu Gln Val Gln Val 65
 Val Leu Pro Leu Leu Pro Leu Leu Gln Gly Ser Gly Lys Ser Asn Val 80
 Val Ala Trp Gly Asp Tyr Asp Asp Ser Ala Phe Met Asp Pro Arg Tyr 95
 His Val His Gly Glu Asp Leu Asp Lys Leu His Arg Ala Ala Trp Trp 110
 Gly Lys Val Pro Arg Lys Asp Leu Ile Val Met Leu Arg Asp Thr Asp 125
 Val Asn Lys Arg Asp Lys Gln Lys Arg Thr Ala Leu His Leu Ala Ser 140

145	150	155	160
Ala Asn Gly Asn Ser Glu Val Val Lys Leu Val Leu Asp Arg Arg Cys			
	165	170	175
Gln Leu Asn Val Leu Asp Asn Lys Lys Arg Thr Ala Leu Thr Lys Ala			
	180	185	190
Val Gln Cys Gln Glu Asp Glu Cys Ala Leu Met Leu Leu Glu His Gly			
	195	200	205
Thr Asp Pro Asn Ile Pro Asp Glu Tyr Gly Asn Thr Thr Leu His Tyr			
	210	215	220
Ala Val Tyr Asn Glu Asp Lys Leu Met Ala Lys Ala Leu Leu Leu Tyr			
	225	230	235
Gly Ala Asp Ile Glu Ser Lys Asn Lys His Gly Leu Thr Pro Leu Leu			
	245	250	255
Leu Gly Ile His Glu Gln Lys Gln Gln Val Val Lys Phe Leu Ile Lys			
	260	265	270
Lys Lys Ala Asn Leu Asn Ala Leu Asp Arg Tyr Gly Arg Thr Ala Leu			
	275	280	285
Ile Leu Ala Val Cys Cys Gly Ser Ala Ser Ile Val Ser Pro Leu Leu			
	290	295	300
Glu Gln Asn Val Asp Val Ser Ser Gln Asp Leu Glu Arg Arg Pro Glu			
	305	310	315
Ser Met Leu Phe Leu Val Ile Ile Met			320

325

<210> 300

<211> 148

<212> PRT

<213> Homo sapien

<220>

<221> VARIANT

<222> (1)...(148)

<223> Xaa = Any Amino Acid

<400> 300

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Trp Thr Ser Ser Thr Glu Leu Pro Trp Trp Gly Lys Val Pro Arg Lys			
	20	25	30
Asp Leu Ile Val Met Leu Arg Asp Thr Asp Val Asn Lys Xaa Asp Lys			
	35	40	45
Gln Lys Arg Thr Ala Leu His Leu Ala Ser Ala Asn Gly Asn Ser Glu			
	50	55	60
Val Val Lys Leu Xaa Leu Asp Arg Arg Cys Gln Leu Asn Val Leu Asp			
	65	70	75
Asn Lys Lys Arg Thr Ala Leu Xaa Lys Ala Val Gln Cys Gln Glu Asp			
	85	90	95
Glu Cys Ala Leu Met Leu Leu Glu His Gly Thr Asp Pro Asn Ile Pro			
	100	105	110
Asp Glu Tyr Gly Asn Thr Thr Leu His Tyr Ala Xaa Tyr Asn Glu Asp			
	115	120	125
Lys Leu Met Ala Lys Ala Leu Leu Leu Tyr Gly Ala Asp Ile Glu Ser			
	130	135	140
Lys Asn Lys Val			
145			

<210> 301
 <211> 1155
 <212> DNA
 <213> Homo sapien

<400> 301

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ggcgcttctg	gagaccacga	cgactctgct	atgaagacac	tcaggaacaa	gatgggcaag	300
tggtgctgcc	actgcttccc	ctgctgcagg	gggagcggca	agagcaaggt	gggcgcttgg	360
ggagactacg	atgacagtgc	cttcatggag	cccaggtagc	acgtccgtgg	agaagatctg	420
gacaagctcc	acagagctgc	ctggtggggg	aaagtcccca	gaaaggatct	catcgtcatg	480
ctcagggaca	ctgacgtgaa	caagaaggac	aagcaaaaga	ggactgctct	acatctggcc	540
tctgccaatg	ggaattcaga	agtagtaaaa	ctcctgctgg	acagacgatg	tcaacttaat	600
gtccttgaca	acaaaaagag	gacagctctg	ataaaggccg	tacaatgcta	ggaagatgaa	660
tgtgcgttaa	tggtgctgga	acatggcact	gatccaaata	ttccagatga	gtatggaaat	720
accactctgc	actacgctat	ctataatgaa	gataaattaa	tggccaaagc	actgctctta	780
tatggtgctg	atatcgaatc	aaaaaacaag	catggcctca	caccactgtt	acttgggtgta	840
catgagcaaa	aacagcaagt	cgtgaaatct	ttaatcaaga	aaaaagcgaa	tttaaatgca	900
ctggatagat	atggaaggac	tgctctcata	cttgcgtgat	gttgtggatc	agcaagtata	960
gtcagccttc	tacttgagca	aaatattgat	gtatcttctc	aagatctatc	tggaagagcg	1020
gccagagagt	atgctgtttc	tagtcacatc	catgtaattt	gccagttact	ttctgactac	1080
aaagaaaaac	agatgctaaa	aatctcttct	gaaaacagca	atccagaaaa	tgtctcaaga	1140
accagaaata	aataa					1155

<210> 302
 <211> 2000
 <212> DNA
 <213> Homo sapien

<400> 302

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agcaacgttg	gcacttctgg	agaccacgac	gactctgcta	tgaagacact	caggagcaag	180
atgggcaagt	ggtgccgcca	ctgcttcccc	tgctgcaggg	ggagtggcaa	gagcaacgtg	240
ggcgcttctg	gagaccacga	cgactctgct	atgaagacac	tcaggaacaa	gatgggcaag	300
tggtgctgcc	actgcttccc	ctgctgcagg	gggagcggca	agagcaaggt	gggcgcttgg	360
ggagactacg	atgacagtgc	cttcatggag	cccaggtagc	acgtccgtgg	agaagatctg	420
gacaagctcc	acagagctgc	ctggtggggg	aaagtcccca	gaaaggatct	catcgtcatg	480
ctcagggaca	ctgacgtgaa	caagaaggac	aagcaaaaga	ggactgctct	acatctggcc	540
tctgccaatg	ggaattcaga	agtagtaaaa	ctcctgctgg	acagacgatg	tcaacttaat	600
gtccttgaca	acaaaaagag	gacagctctg	ataaaggccg	tacaatgcca	ggaagatgaa	660
tgtgcgttaa	tggtgctgga	acatggcact	gatccaaata	ttccagatga	gtatggaaat	720
accactctgc	actacgctat	ctataatgaa	gataaattaa	tggccaaagc	actgctctta	780
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catgagcaaa	aacagcaagt	cgtgaaatct	ttaatcaaga	aaaaagcgaa	tttaaatgca	900
ctggatagat	atggaaggac	tgctctcata	cttgcgtgat	gttgtggatc	agcaagtata	960
gtcagccttc	tacttgagca	aaatattgat	gtatcttctc	aagatctatc	tggaagagcg	1020
gccagagagt	atgctgtttc	tagtcacatc	catgtaattt	gccagttact	ttctgactac	1080
aaagaaaaac	agatgctaaa	aatctcttct	gaaaacagca	atccagaaaa	agacttaaaag	1140
ctgacatcag	aggaagagtc	acaaagggtc	aaaggcagtg	aaaatagcca	gccagagaaa	1200
atgtctcaag	aaccagaaat	aaataaggat	ggtgatagag	agggtgaaga	agaaatgaag	1260

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<210> 303

<211> 2040

<212> DNA

<213> Homo sapien

<400> 303

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 ggagactacg atgacagtgc cttcatggag cccagggtacc acgtccgtgg agaagatctg 420
 gacaagctcc acagagctgc ctggtggggg aaagtcccc gaaaggatct catcgatctg 480
 ctgagggaca ctgacgtgaa caagaaggac aagcaaaaga ggactgctct acatctggcc 540
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 gtccttgaca acaaaaagag gacagctctg ttaaaaggcg tacaatgcca ggaagatgaa 660
 tgtgcgttaa tgttgctgga acatggcact gatccaaata ttccagatga gtatggaaat 720
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 gaaaagcaga tagaagtggg tgaaaaaatg aattctgagc ttctcttag ttgtaagaaa 1920
 gaaaagaca tcttgcatga aaatagtacg ttgcgggaag aaattgccat gctaagactg 1980
 gagctagaca caatgaaca tcagagccag ctaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 2040

<210> 304
 <211> 384
 <212> PRT
 <213> Homo sapiens
 <400> 304
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 Pro Cys Cys Arg Glu Ser Gly Lys Ser Asn Val Gly Thr Ser Gly Asp
 35 40 45
 His Asp Asp Ser Ala Met Lys Thr Leu Arg Ser Lys Met Gly Lys Trp
 50 55 60
 Cys Arg His Cys Phe Pro Cys Cys Arg Gly Ser Gly Lys Ser Asn Val
 65 70 75 80
 Gly Ala Ser Gly Asp His Asp Asp Ser Ala Met Lys Thr Leu Arg Asn
 85 90 95
 Lys Met Gly Lys Trp Cys Cys His Cys Phe Pro Cys Cys Arg Gly Ser
 100 105 110
 Gly Lys Ser Lys Val Gly Ala Trp Gly Asp Tyr Asp Asp Ser Ala Phe
 115 120 125
 Met Glu Pro Arg Tyr His Val Arg Gly Glu Asp Leu Asp Lys Leu His
 130 135 140
 Arg Ala Ala Trp Trp Gly Lys Val Pro Arg Lys Asp Leu Ile Val Met
 145 150 155
 Leu Arg Asp Thr Asp Val Asn Lys Lys Asp Lys Gln Lys Arg Thr Ala
 160 165 170 175
 Leu His Leu Ala Ser Ala Asn Gly Asp Ser Glu Val Val Lys Leu Leu
 180 185 190
 Leu Asp Arg Arg Cys Gln Leu Asp Val Ser Asp Asn Lys Lys Arg Thr
 195 200 205
 Ala Leu Ile Lys Ala Val Gln Cys Gln Glu Asp Glu Cys Ala Leu Met
 210 215 220
 Leu Leu Glu His Gly Thr Asp Pro Asn Ile Pro Asp Glu Tyr Gly Asn
 225 230 235 240
 Thr Thr Leu His Tyr Ala Ile Tyr Asn Glu Asp Lys Leu Met Ala Lys
 245 250 255
 Ala Leu Leu Tyr Gly Ala Asp Ile Glu Ser Lys Asn Lys His Gly
 260 265 270
 Leu Thr Pro Leu Leu Leu Gly Val His Glu Gln Lys Gln Gln Val Val
 275 280 285
 Lys Phe Leu Ile Lys Lys Lys Ala Asp Leu Asn Ala Leu Asp Arg Tyr
 290 295 300
 Gly Arg Thr Ala Leu Ile Leu Ala Val Cys Cys Gly Ser Ala Ser Ile
 305 310 315 320
 Val Ser Leu Leu Leu Glu Gln Asn Ile Asp Val Ser Ser Gln Asp Leu
 325 330 335
 Ser Gly Gln Thr Ala Arg Glu Tyr Ala Val Ser Ser His His His Val
 340 345 350
 Ile Cys Gln Leu Leu Ser Asp Tyr Lys Glu Lys Gln Met Leu Lys Ile
 355 360 365
 Ser Ser Glu Asn Ser Asn Pro Glu Asn Val Ser Arg Thr Arg Asn Lys
 370 375 380

<210> 305

<211> 656

<212> PRT

<213> Homo sapien

<400> 305

Met Val Val Glu Val Asp Ser Met Pro Ala Ala Ser Ser Val Lys Lys
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 20 25 30
 Pro Cys Cys Arg Glu Ser Gly Lys Ser Asn Val Gly Thr Ser Gly Asp
 35 40 45
 His Asp Asp Ser Ala Met Lys Thr Leu Arg Ser Lys Met Gly Lys Trp
 50 55 60
 Cys Arg His Cys Phe Pro Cys Cys Arg Gly Ser Gly Lys Ser Asn Val
 65 70 75 80
 Gly Ala Ser Gly Asp His Asp Asp Ser Ala Met Lys Thr Leu Arg Asn
 85 90 95
 Lys Met Gly Lys Trp Cys Cys His Cys Phe Pro Cys Cys Arg Gly Ser
 100 105 110
 Gly Lys Ser Lys Val Gly Ala Trp Gly Asp Tyr Asp Asp Ser Ala Phe
 115 120 125
 Met Glu Pro Arg Tyr His Val Arg Gly Glu Asp Leu Asp Lys Leu His
 130 135 140
 Arg Ala Ala Trp Trp Gly Lys Val Pro Arg Lys Asp Leu Ile Val Met
 145 150 155 160
 Leu Arg Asp Thr Asp Val Asn Lys Lys Asp Lys Gln Lys Arg Thr Ala
 165 170 175
 Leu His Leu Ala Ser Ala Asn Gly Asn Ser Glu Val Val Lys Leu Leu
 180 185 190
 Leu Asp Arg Arg Cys Gln Leu Asn Val Leu Asp Asn Lys Lys Arg Thr
 195 200 205
 Ala Leu Ile Lys Ala Val Gln Cys Gln Glu Asp Glu Cys Ala Leu Met
 210 215 220
 Leu Leu Glu His Gly Thr Asp Pro Asn Ile Pro Asp Glu Tyr Gly Asn
 225 230 235 240
 Thr Thr Leu His Tyr Ala Ile Tyr Asn Glu Asp Lys Leu Met Ala Lys
 245 250 255
 Ala Leu Leu Leu Tyr Gly Ala Asp Ile Glu Ser Lys Asn Lys His Gly
 260 265 270
 Leu Thr Pro Leu Leu Leu Gly Val His Glu Gln Lys Gln Gln Val Val
 275 280 285
 Lys Phe Leu Ile Lys Lys Lys Ala Asn Leu Asn Ala Leu Asp Arg Tyr
 290 295 300
 Gly Arg Thr Ala Leu Ile Leu Ala Val Cys Cys Gly Ser Ala Ser Ile
 305 310 315 320
 Val Ser Leu Leu Leu Glu Gln Asn Ile Asp Val Ser Ser Gln Asp Leu
 325 330 335
 Ser Gly Gln Thr Ala Arg Glu Tyr Ala Val Ser Ser His His His Val
 340 345 350
 Ile Cys Gln Leu Leu Ser Asp Tyr Lys Glu Lys Gln Met Leu Lys Ile
 355 360 365
 Ser Ser Glu Asn Ser Asn Pro Glu Gln Asp Leu Lys Leu Thr Ser Glu
 370 375 380
 Glu Glu Ser Gln Arg Phe Lys Gly Ser Glu Asn Ser Gln Pro Glu Lys

385 390 395 400
 Met Ser Gln Glu Pro Glu Ile Asn Lys Asp Gly Asp Arg Glu Val Glu
 405 410 415
 Glu Glu Met Lys Lys His Glu Ser Asn Asn Val Gly Leu Leu Glu Asn
 420 425 430
 Leu Thr Asn Gly Val Thr Ala Gly Asn Gly Asp Asn Gly Leu Ile Pro
 435 440 445
 Gln Arg Lys Ser Arg Thr Pro Glu Asn Gln Gln Phe Pro Asp Asn Glu
 450 455 460
 Ser Glu Glu Tyr His Arg Ile Cys Glu Leu Val Ser Asp Tyr Lys Glu
 465 470 475 480
 Lys Gln Met Pro Lys Tyr Ser Ser Glu Asn Ser Asn Pro Glu Gln Asp
 485 490 495
 Leu Lys Leu Thr Ser Glu Glu Glu Ser Gln Arg Leu Glu Gly Ser Glu
 500 505 510
 Asn Gly Gln Pro Glu Leu Glu Asn Phe Met Ala Ile Glu Glu Met Lys
 515 520 525
 Lys His Gly Ser Thr His Val Gly Phe Pro Glu Asn Leu Thr Asn Gly
 530 535 540
 Ala Thr Ala Gly Asn Gly Asp Asp Gly Leu Ile Pro Pro Arg Lys Ser
 545 550 555 560
 Arg Thr Pro Glu Ser Gln Gln Phe Pro Asp Thr Glu Asn Glu Glu Tyr
 565 570 575
 His Ser Asp Glu Gln Asn Asp Thr Gln Lys Gln Phe Cys Glu Glu Gln
 580 585 590
 Asn Thr Gly Ile Leu His Asp Glu Ile Leu Ile His Glu Glu Lys Gln
 595 600 605
 Ile Glu Val Val Glu Lys Met Asn Ser Glu Leu Ser Leu Ser Cys Lys
 610 615 620
 Lys Glu Lys Asp Ile Leu His Glu Asn Ser Thr Leu Arg Glu Glu Ile
 625 630 635 640
 Ala Met Leu Arg Leu Glu Leu Asp Thr Met Lys His Gln Ser Gln Leu
 645 650 655

<210> 306

<211> 671

<212> PRT

<213> Homo sapien

<400> 306

Met Val Val Glu Val Asp Ser Met Pro Ala Ala Ser Ser Val Lys Lys
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 Pro Phe Gly Leu Arg Ser Lys Met Gly Lys Trp Cys Cys Arg Cys Phe
 20 25 30
 Pro Cys Cys Arg Glu Ser Gly Lys Ser Asn Val Gly Thr Ser Gly Asp
 35 40 45
 His Asp Asp Ser Ala Met Lys Thr Leu Arg Ser Lys Met Gly Lys Trp
 50 55 60
 Cys Arg His Cys Phe Pro Cys Cys Arg Gly Ser Gly Lys Ser Asn Val
 65 70 75 80
 Gly Ala Ser Gly Asp His Asp Asp Ser Ala Met Lys Thr Leu Arg Asn
 85 90 95
 Lys Met Gly Lys Trp Cys Cys His Cys Phe Pro Cys Cys Arg Gly Ser
 100 105 110
 Gly Lys Ser Lys Val Gly Ala Trp Gly Asp Tyr Asp Asp Ser Ala Phe

115 120 125
 Met Glu Pro Arg Tyr His Val Arg Gly Glu Asp Leu Asp Lys Leu His
 130 135 140
 Arg Ala Ala Trp Trp Gly Lys Val Pro Arg Lys Asp Leu Ile Val Met
 145 150 155 160
 Leu Arg Asp Thr Asp Val Asn Lys Lys Asp Lys Gln Lys Arg Thr Ala
 165 170 175
 Leu His Leu Ala Ser Ala Asn Gly Asn Ser Glu Val Val Lys Leu Leu
 180 185 190
 Leu Asp Arg Arg Cys Gln Leu Asn Val Leu Asp Asn Lys Lys Arg Thr
 195 200 205
 Ala Leu Ile Lys Ala Val Gln Cys Gln Glu Asp Glu Cys Ala Leu Met
 210 215 220
 Leu Leu Glu His Gly Thr Asp Pro Asn Ile Pro Asp Glu Tyr Gly Asn
 225 230 235 240
 Thr Thr Leu His Tyr Ala Ile Tyr Asn Glu Asp Lys Leu Met Ala Lys
 245 250 255
 Ala Leu Leu Leu Tyr Gly Ala Asp Ile Glu Ser Lys Asn Lys His Gly
 260 265 270
 Leu Thr Pro Leu Leu Leu Gly Val His Glu Gln Lys Gln Gln Val Val
 275 280 285
 Lys Phe Ile Lys Lys Lys Ala Asn Leu Asn Ala Leu Asp Arg Tyr
 290 295 300
 Gly Arg Ala Leu Ile Leu Ala Val Cys Cys Gly Ser Ala Ser Ile
 305 310 315 320
 Val Ser Leu Leu Glu Gln Asn Ile Asp Val Ser Ser Gln Asp Leu
 325 330 335
 Ser Gly Gln Thr Ala Arg Glu Tyr Ala Val Ser Ser His His His Val
 340 345 350
 Ile Cys Gln Leu Leu Ser Asp Tyr Lys Glu Lys Gln Met Leu Lys Ile
 355 360 365
 Ser Ser Glu Asn Ser Asn Pro Glu Gln Asp Leu Lys Leu Thr Ser Glu
 370 375 380
 Glu Glu Ser Gln Arg Phe Lys Gly Ser Glu Asn Ser Gln Pro Glu Lys
 385 390 395 400
 Met Ser Gln Glu Pro Glu Ile Asn Lys Asp Gly Asp Arg Glu Val Glu
 405 410 415
 Glu Glu Met Lys Lys His Glu Ser Asn Asn Val Gly Leu Leu Glu Asn
 420 425 430
 Leu Thr Asn Gly Val Thr Ala Gly Asn Gly Asp Asn Gly Leu Ile Pro
 435 440 445
 Gln Arg Lys Ser Arg Thr Pro Glu Asn Gln Gln Phe Pro Asp Asn Glu
 450 455 460
 Ser Glu Glu Tyr His Arg Ile Cys Glu Leu Val Ser Asp Tyr Lys Glu
 465 470 475 480
 Lys Gln Met Pro Lys Tyr Ser Ser Glu Asn Ser Asn Pro Glu Gln Asp
 485 490 495
 Leu Lys Leu Thr Ser Glu Glu Glu Ser Gln Arg Leu Glu Gly Ser Glu
 500 505 510
 Asn Gly Gln Pro Glu Lys Arg Ser Gln Glu Pro Glu Ile Asn Lys Asp
 515 520 525
 Gly Asp Arg Glu Leu Glu Asn Phe Met Ala Ile Glu Glu Met Lys Lys
 530 535 540
 His Gly Ser Thr His Val Gly Phe Pro Glu Asn Leu Thr Asn Gly Ala
 545 550 555 560

Thr Ala Gly Asn Gly Asp Asp Gly Leu Ile Pro Pro Arg Lys Ser Arg
 565 570 575
 Thr Pro Glu Ser Gln Gln Phe Pro Asp Thr Glu Asn Glu Glu Tyr His
 580 585 590
 Ser Asp Glu Gln Asn Asp Thr Gln Lys Gln Phe Cys Glu Glu Gln Asn
 595 600 605
 Thr Gly Ile Leu His Asp Glu Ile Leu Ile His Glu Glu Lys Gln Ile
 610 615 620
 Glu Val Val Glu Lys Met Asn Ser Glu Leu Ser Leu Ser Cys Lys Lys
 625 630 635 640
 Glu Lys Asp Ile Leu His Glu Asn Ser Thr Leu Arg Glu Glu Ile Ala
 645 650 655
 Met Leu Arg Leu Glu Leu Asp Thr Met Lys His Gln Ser Gln Leu
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 <210> 307
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 <212> DNA
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CONFIDENTIAL - SECURITY INFORMATION

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39/395, 48/00, C12N 5/08, G01N 33/574, C12Q 1/68

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ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS,
LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ,
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(84) Designated States (*regional*): ARIPO patent (GH, GM,
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(AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU,
MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM,
GA, GN, GW, ML, MR, NE, SN, TD, TG).

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Published:

— With international search report.

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(88) Date of publication of the international search report:
28 June 2001

For two-letter codes and other abbreviations, refer to the "Guid-
ance Notes on Codes and Abbreviations" appearing at the begin-
ning of each regular issue of the PCT Gazette.

(54) Title: COMPOSITIONS AND METHODS FOR THE TREATMENT AND DIAGNOSIS OF BREAST CANCER



cDNA PREPARED FROM
NORMAL BREAST TISSUE
FROM THE SAME PATIENT

cDNA PREPARED
FROM BREAST TUMOR

B18Ag1

(57) Abstract: Compositions and methods for the detection and therapy of breast cancer are disclosed. The compounds provided include nucleotide sequences that are preferentially expressed in breast tumor tissue, as well as polypeptides encoded by such nucleotide sequences. Vaccines and pharmaceutical compositions comprising such compounds are also provided and may be used, for example, for the prevention and treatment of breast cancer. The polypeptides may also be used for the production of antibodies, which are useful for diagnosing and monitoring the progression of breast cancer in a patient.

WO 00/61753 A3

INTERNATIONAL SEARCH REPORT

Int. Application No

PCT/US 00/09312

A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 C12N15/12 C07K14/47 C07K16/18 C07K19/00 C12N15/62
 A61K38/17 A61K39/395 A61K48/00 C12N5/08 G01N33/574
 C12Q1/68

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 C12N C07K A61K G01N C12Q

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the International search (name of data base and, where practical, search terms used)

EPO-Internal

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 98 45328 A (CORIXA CORPORATION) 15 October 1998 (1998-10-15) page 2, line 7 -page 5, line 22 page 7, line 23 -page 24, line 11; examples 1-4 sequence listing SEQ ID NOs:1, 3-10, 227 ---	1,2,4-60
X	WO 97 25426 A (CORIXA CORPORATION) 17 July 1997 (1997-07-17) page 2, line 8 -page 5, line 11 page 7, line 14 -page 23, line 2; example 1 sequence listing SEQ ID NO:1, 3-10, 227 ---	1,2,4-60
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☒ Further documents are listed in the continuation of box C.☒ Patent family members are listed in annex.

* Special categories of cited documents:

- "A" document defining the general state of the art which is not considered to be of particular relevance
- "E" earlier document but published on or after the international filing date
- "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- "O" document referring to an oral disclosure, use, exhibition or other means
- "P" document published prior to the international filing date but later than the priority date claimed

- "T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- "X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- "Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- "&" document member of the same patent family

Date of the actual completion of the international search

8 August 2000

Date of mailing of the international search report

08.11.00

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2
 NL - 2280 HV Rijswijk

Authorized officer

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	<p>WO 97 25431 A (CORIXA CORPORATION) 17 July 1997, (1997-07-17) page 2, line 3 -page 3, line 25 page 4, line 12 -page 17, line 18; examples 1-4 sequence listing SEQ ID NOs:1, 3-10</p>	<p>1,2,4-10</p>

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US 00/09312

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☒ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

Although claims 21, 22, 29-31 34 37-39 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.
2. ☐ Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this International application, as follows:

see additional sheet

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☒ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Claims 1, 2, 4-60 Partially.

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. Claims: Partially 1, 2, 4-60

Breast cancer related polypeptide B18Ag1; corresponding polynucleotides comprising SEQ ID NOs:1, 3-10, or 227, and derived oligonucleotides; variants thereof, expression vector and host cell comprising the same; antibody and diagnostic kit containing it, fusion protein comprising the polypeptide; pharmaceutical composition and vaccine comprising any of the above and use therefor in the treatment of cancer, and for removing tumor cells from a sample; use of the polypeptides for stimulating and expanding T-cells and use of such T-cells for inhibiting cancer development; use of the polypeptides for determining the presence of cancer or monitoring the progression of cancer in a patient.

2. Claims: Partially 1-60

Idem as subject 1 for Breast cancer related polypeptide and polynucleotide B21GT2 (B311D) comprising SEQ ID NOs:56, 307, 308, 316 or 317.

3. Claims: Partially 1, 2, 4-60

Idem as subject 1 for Breast cancer related polypeptide and polynucleotide B15Ag1 comprising SEQ ID NOs:27 or 290.

4. Claims: Partially 1, 2, 4-60

Idem as subject 1 for Breast cancer related polypeptide and polynucleotide B31GA1b comprising SEQ ID NOs:148.

5. Claims: Partially 1, 2, 4-60

Idem as subject 1 for Breast cancer related polypeptide and polynucleotide B38GA2a comprising SEQ ID NOs:157.

6. Claims: Partially 1-60

Idem as subject 1 for Breast cancer related polypeptide and polynucleotide B11Ag1 (B305D) and its isoform A comprising SEQ ID NO:292-306, or 309-315.

7. Claims: Claims: Partially 1, 2, 4-60,
all as far as applicable

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Breast cancer related polypeptides, corresponding polynucleotides comprising SEQ ID NOs:11-26 (inventions 7-22), 28-55 (inventions 23-50), 57-86 (inventions 51-80), 142-147 (inventions 81-86), 149-156 (inventions 87-94), 158-226 (inventions 95-163), 228-253 (inventions 164-189), or 255-291 (inventions 190-226), and derived oligonucleotides; variants thereof, expression vector and host cell comprising the same; antibody and diagnostic kit containing it, fusion protein comprising the polypeptide; pharmaceutical composition and vaccine comprising any of the above and use therefor in the treatment of cancer, and for removing tumor cells from a sample; use of the polypeptides for stimulating and expanding T-cells and use of such T-cells for inhibiting cancer development; use of the polypeptides for inhibiting or monitoring the progression of cancer in a patient, as far as applicable.

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 9845328 A	15-10-1998	AU 6956098 A EP 0975666 A NO 994932 A PL 336349 A ZA 9802968 A	30-10-1998 02-02-2000 07-12-1999 19-06-2000 27-10-1998
WO 9725426 A	17-07-1997	AU 1697497 A BR 9707125 A CA 2242340 A CN 1211279 A EP 0874902 A NO 983183 A	01-08-1997 20-07-1999 17-07-1997 17-03-1999 04-11-1998 10-09-1998
WO 9725431 A	17-07-1997	AU 1575697 A	01-08-1997

Form PCT/ISA/210 (patent family annex) (July 1992)